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The American Academy of Pediatrics

October 18 to 23, 1952

Palmer House

Chicago

AREAL MEETING

May 22 to 24, 1952

Statler Hotel

Washington, D.C.

Pediatrics

VOLUME 9 MAY 1952 NUMBER 5, PART I

ORIGINAL ARTICLES

THERAPEUTIC MEASURES PROMOTING RECOVERY FROM THE PHYSIOLOGIC DISTURBANCES OF INFANTILE DIARRHEA

By DANIEL C. DARROW, M.D.
New Haven, Conn.

ALTHOUGH the improvements in fluid therapy have seemed to result largely from recent clinical observations, actually the fundamental ideas were developed by research on experimental animals in laboratories of physiology, biochemistry, pharmacology and clinical medicine. In many aspects, the progress has depended on laboratory work using physiologic and biochemical methods but applied with a point of view arising from clinical experience. The opportunities for this type of research came largely with full-time medicine in clinical departments.

I was led to the use of potassium in fluid therapy by studies which were carried out on experimental animals throughout a period of 10 years in association with Drs. Yannet, Harrison and Miller. We had the excellent technical assistance of Miss Carey, Miss Coville and Mr. Iannucci and Mr. Barringham. During these years, the knowledge of the metabolism of water and electrolyte was advancing rapidly under the leadership of Gamble, Van Slyke, Peters, Loeb, Hastings, Fenn, Adolph, Butler, Homer Smith, and Newburg to mention only a few. In 1945, I summarized this knowledge of body water and electrolytes as related to clinical problems.[1] Through the courtesy of Dr. Park, I came to Baltimore on VJ day to work for 60 days with the facilities of the pediatric department at Johns Hopkins. The study of diarrhea was made possible by the nurses, the resident, Dr. Govan, the head of the laboratory, Dr. Kaydi, and a superb technician, Mrs. Radcliffe. Through Hansen's generosity, Flett, Pratt, Wiese, Alice Gamble and I later extended these observations in Texas. We were able to show that deficiency of potassium occurs in diarrhea, that potassium may safely be used parenterally or orally and that improved results follow its use. From all this it can be seen that the selection of one man for the Borden award places his work out of context. Any work which I have done was

Borden Award Address, read at the Annual Meeting, American Academy of Pediatrics, Toronto, Oct. 24, 1951.

From the Yale University School of Medicine, New Haven, Conn.

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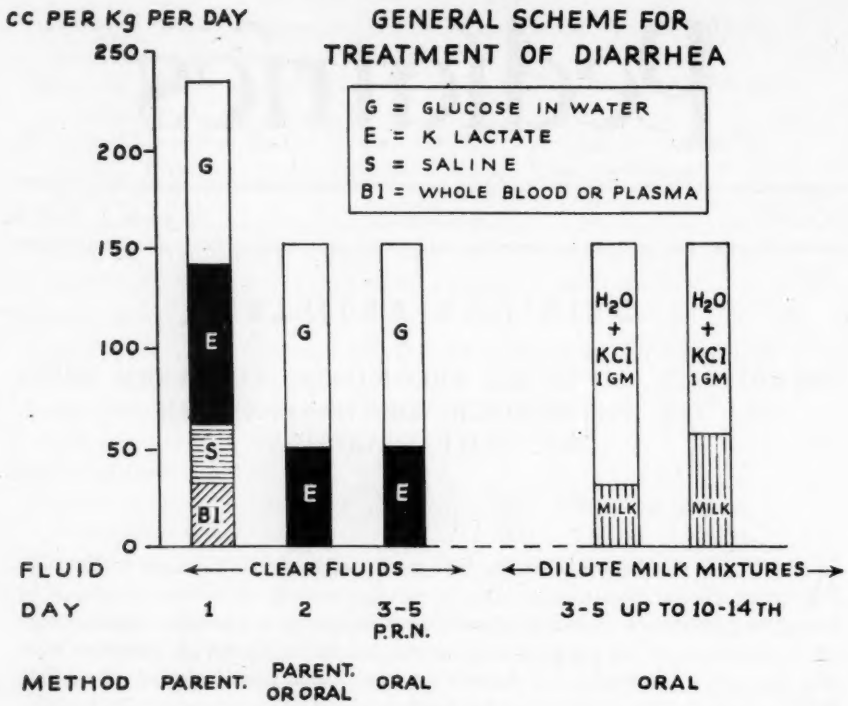

CHART 1

dependent on my associates and the investigations of other laboratories. I owe more to Grover F. Powers than anyone for, in applying laboratory work to clinical medicine, no help is as much needed as the knowledge and judgment of the course of disease that only a supreme clinician possesses. Furthermore, I have been able to do work with no obvious immediate goal because I was supported by the University for just that purpose and was not required to sign the essentially false promissory notes involved in project research which is the fashion today.

Although the addition of potassium increased the effectiveness of treatment of diarrhea, Govan and I believed it should be introduced as a part of the previously established therapeutic program. At present the problem is to achieve a proper balance in the utilization of the various procedures. For this reason, I shall review the physiologic and clinical basis of our therapeutic program. If I am able to present a sound physiologic basis for the various therapeutic procedures, I shall achieve my purpose of showing how a balanced and comprehensive therapeutic program can be planned.

Chart 1 shows our outline of the treatment of severe dehydration due to diarrhea. The actual procedures vary a good deal with the severity of the illness and the reaction of the patient. The important steps are as follows:

1. Reduction of abnormal losses of water and electrolyte by withholding all oral fluids as long as they are likely to be vomited and the omission of milk feeding for 24 hours or until it is unlikely greatly to increase stool volume.

2. In severe cases, the administration of all fluids parenterally for 24 hours. The solutions should provide enough Na, Cl and water to replace the deficits and cover a high rate of expenditure of these substances. Potassium should also be given to cover a high rate of expenditure and maintain serum concentrations. The total fluid intake should seldom be less than 200 cc./kg. body weight during the first day and some cases will require 300 to 350 cc.

3. Treatment of incipient as well as manifest shock as soon as possible with an infusion of lactate ringer's solution followed by a transfusion of blood.

4. After the first day in severe cases, body water and electrolyte can usually be main-

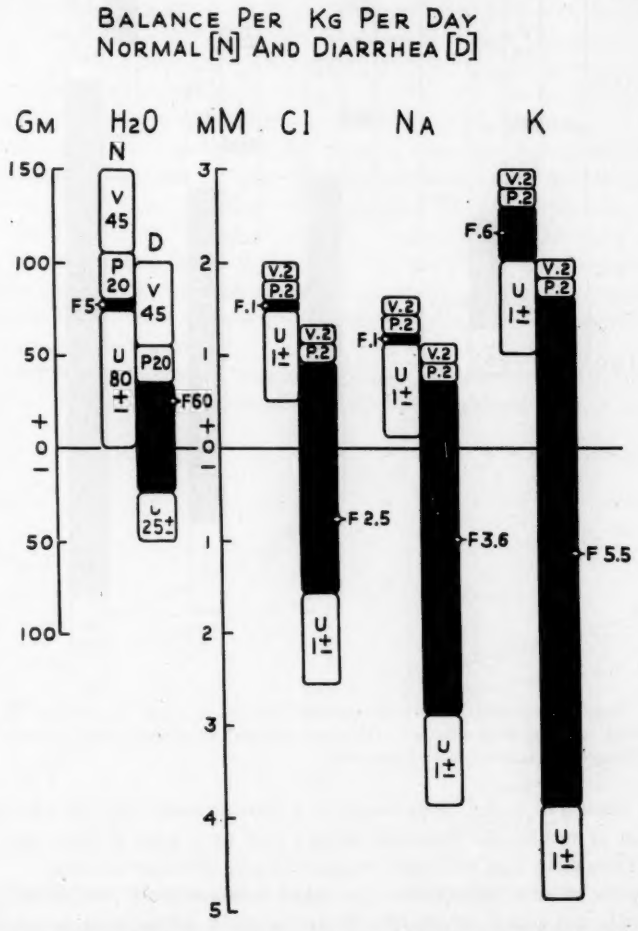

CHART 2. Diagram represents factors determining balances of water, Cl, Na and K in normal (N) and infants suffering from diarrhea (D) when sweat volumes are low. Intake is indicated by height of column above base line. Output is measured down from intake so that retention is indicated above base line and loss, below base line. v indicates losses from lungs and skin when there is no sweat; P, losses in sweat; F, stool losses and U, urine losses.

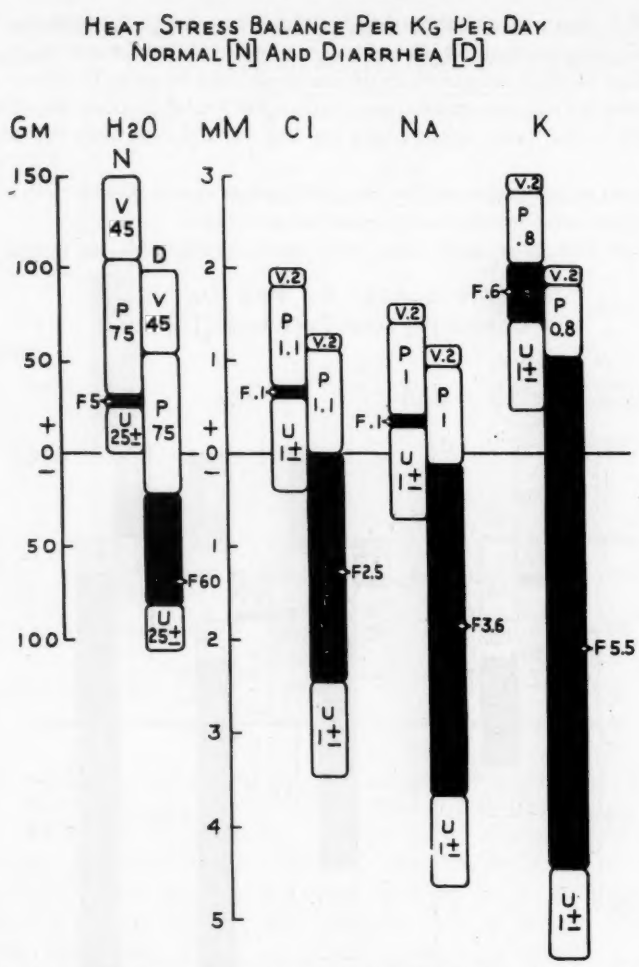

CHART 3. Diagram represents factors determining balances of water, Cl, Na and K in normal (N) and infants suffering from diarrhea (D) when temperature produces large volumes of sweat. Diagram is constructed in same manner as that of chart 2.

tained with about 150 cc./kg. body weight of a mixture containing Na, Cl and K and glucose given by mouth. All parenteral therapy may be omitted by using this solution at the start of treatment in all mild cases and in many moderately severe ones.

5. Resumption of milk feeding after a period of fasting of from 1 to 5 days. A suitable mixture of milk and added carbohydrate should be given diluted so as to contain 10 to 20 calories and 150 cc. of fluid/kg. body weight on the first day. The intake of milk mixture is increased about 20 calories/kg. each day until 90 to 100 calories/kg. body weight per day are taken. Total fluid intake is kept constant as caloric intake is increased.

The above outline cannot be applied intelligently without understanding (1) the

factors leading to losses of body water and electrolyte, (2) the magnitude of the losses of body water and electrolyte, (3) the disturbances such as shock and acidosis resulting from losses of body water and electrolyte and (4) the role of food in aggravating losses of water and electrolyte in the stools. The subsequent part of the paper considers these aspects of diarrhea.

The mechanism of the development of deficits of water and electrolyte in diarrhea is illustrated in charts 2 and 3. The intake on a milk mixture providing one third of the calories in added carbohydrate is compared to the outputs by the lungs and skin, the stools and urine. The normal subject is contrasted with one with severe diarrhea. It is assumed that each day about 20 cc. of sweat is being formed/kg. body weight at the usual room temperature. The increase in stool water and electrolyte is compensated for as far as possible by diminished urine losses during diarrhea. The stool water and electrolyte were calculated from representative volumes and concentrations reported by Holt, Courtney and Fales.[2] It is assumed that the intake during diarrhea decreases to two thirds of the normal intake. As may be seen, the losses of electrolyte are somewhat greater than the relative losses of water and lead to hypotonic dehydration. Since diarrhea produces notoriously more serious disturbances in hot weather, the effect of heat stress and diarrhea are illustrated in chart 3. The volume of sweat was assumed to be 75 cc./kg. body weight/day—a rate of sweating found at about 33.8°C. The relative rates of loss of water and electrolyte indicate that hypertonic dehydration would develop. The charts indicate the importance of stool water and electrolyte and the importance of hot weather in aggravating the disturbances of diarrhea.

In the elegant and inimitable language of James L. Gamble,[3] the 1947 Borden lecture pointed out that death in infantile diarrhea may be considered to result from debits ac-

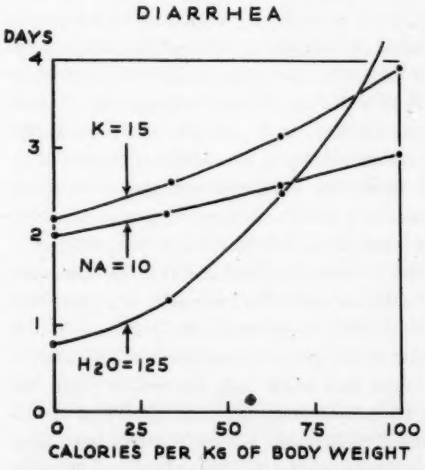

CHART 4. Chart shows time required for accumulation of designated deficits of water, Na and K at varying caloric intakes. Data are based on losses at usual environmental temperatures as in chart 2. Water is expressed in grams and Na and K in mM/kg./body weight.

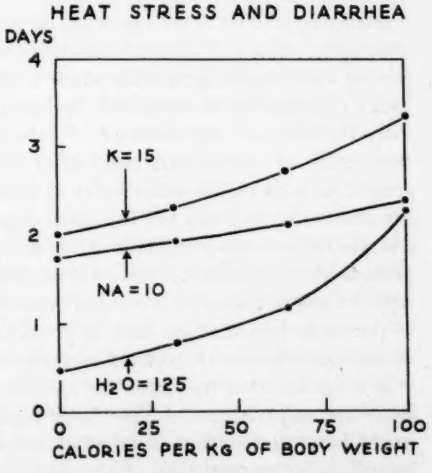

CHART 5. Chart shows time required for accumulation of designated deficits of water, Na and K at environmental temperature inducing large volumes of sweat. Data are based on losses shown in chart 3. Water is expressed in grams and Na and K in mM/kg. body weight.

TABLE 1

RETENTIONS OF WATER AND ELECTROLYTES DURING RECOVERY FROM SEVERE DIARRHEA. WATER IS EXPRESSED IN GRAMS AND ELECTROLYTES IN mM/kg. BODY WEIGHT. (Na)e REFERS TO RETENTIONS IN EXTRACELLULAR FLUIDS AND (Na)i, TO RETENTIONS IN INTRACELLULAR FLUIDS. B^+-Cl INDICATES SUM OF RETENTIONS OF Na AND K MINUS RETENTION OF Cl

	Retentions During Recovery in Diarrhea/kg. Body Weight					
	H_2O	Cl	(Na)e	(Na)i	K	B^+-Cl
	gm.	mM	mM	mM	mM	mM
Av. (8)	125	9	12.8	−3.3	10	11
Max.	200	10	15	3.7	15	16
Min.	85	2	7	−9.5	3	4

cruing from greater expenditure than is restored by intake. Using data like those already shown, charts 4 and 5 were prepared in a similar manner to Gamble's except that the time for accumulation of serious deficits of water, sodium and potassium are shown and calorie deficits are not illustrated. According to Gamble, starvation in well nourished infants produces a deficit in calories which can reach a fatal degree in from 3 to 10 weeks depending on the food intake and the disturbance in absorption. However, since diarrhea attacks undernourished infants and practically no food may be assimilated, death from starvation may result in a few days even if water and electrolyte are maintained. If the ingestion of water and food are reduced proportionally to less than half the normal intake, the deficits of water dominate the picture. This conclusion is based on the fact that only a small part of body water can safely be utilized to meet the large increase in the rate of expenditure of water, whereas considerable amounts of body fat can safely cover a large part of the calorie expenditure which is not increased in diarrhea. As food and water intake is proportionally decreased, fatal deficit of water can develop in from 1 to 10 days. Since the losses of body sodium tend to be parallel to those of water, it can be concluded that deficits of sodium may cause death almost as rapidly if the intake of water is increased so as to replace water losses as when deficits of water and sodium are occurring simultaneously. One may add that losses of potassium are also accumulating at a rapid rate and can lead to serious disorders if not death when these deficits reach a certain extent—perhaps 15 to 20 mM/kg. body weight. Hence if water, sodium and chloride alone are replaced loss of potassium may cause death if diarrhea continues, especially if expenditure of potassium remains high. Loss of potassium is likely to dominate the picture if water, sodium and chloride are replaced and potassium is not given and food is not tolerated.

It is obvious that the charts are arbitrary since they show only the results when the stools are voluminous and have fairly high electrolyte concentrations. Different curves would be obtained with smaller stool volumes. Furthermore, diarrheal stools may have quite different concentrations of electrolyte, some with a great deal of sodium and chloride and less potassium and some with more potassium and less sodium and chloride. Utilization of different stool electrolyte concentrations would alter the time curves for accumulation of serious deficits of the different ions. The charts are meant to illustrate the probable results in quite severe types of diarrhea. Since the slopes of the curves of accumulation of serious deficits of Na and K are not steep, the intake of Na and K in

food is unable to replace the losses in voluminous stools. In other words, improvement in this severe type of diarrhea depends to a great extent on reducing stool losses rather than increasing oral intake. This fact explains why reduction of the rate of expenditure of Na and K by fasting has been so important in treatment. When fasting decreases stool volume, recovery from moderate dehydration is possible on water alone if deficits of electrolyte have not already reached a serious degree. In marked dehydration, the deficits of water and electrolyte must be replaced by appropriate amounts of parenteral fluids or an oral mixture of water and electrolyte that does not seriously increase stool losses.

Table 1 shows the deficits of water and electrolyte in eight cases of diarrhea. The data are based on the balances during recovery reported previously.[4] It is assumed that the retentions which restore the patient measure the deficits leading to the state of dehydration excluding the purely nutritional losses. The estimation of water balance is subject to no great error and may be accepted with considerable confidence. The balances of electrolyte do not include measurements of skin losses. Since the water losses from the lungs and skin could be calculated quite accurately, the increase in these losses above the values which would be obtained when there is no sweating gave a rough estimate of sweat volumes. The concentration of electrolyte in sweat was assumed to be similar to that found in adults. Another difficulty which cannot be readily estimated in these balances arises from the fact that loads of electrolyte temporarily alter balances of these substances.[5] While the retention of sodium, potassium and chloride cannot be considered precise, they are approximately correct since they agree with experimental studies in which the changes in tissue composition are known.[6] The individual values are quite variable. The average water deficit is about 18% of total body water; that of Cl and Na, about one third of extracellular electrolyte; that of potassium about 14% of total body potassium. These values indicate the probable deficits of water and electrolyte in severe dehydration due to infantile diarrhea.

These estimates may be compared to values calculated from charts 2 and 3 for a loss of body water of 125 gm./kg. The predicted deficits agree with those found by the balances during recovery except that chloride losses do not equal those of sodium. However, the data in charts 2 and 3 do not take account of the losses in vomitus nor the compensatory excretion of chloride that is likely to occur in acidosis. For this reason the balance data are apparently correct in finding chloride losses equivalent to sodium losses.

In charts 6 and 7 the probable state of body fluids is shown at a water deficit of 125 gm./kg. body weight when the losses of electrolyte are those in charts 2 and 3 with deficits of Cl equal to those of Na. The state during dehydration is indicated by the solid areas which can be compared to the normal state represented in broken lines. According to the diagram of diarrhea without heat stress, serum chloride concentration remains constant while sodium concentration decreases owing to transfer of sodium to the cells. In diarrhea with heat stress, the concentration of Cl in serum rises somewhat more than that of sodium. The explanation is again transfer of sodium to the cells. Somewhat more water is lost from extracellular fluids when there is no heat stress than during heat stress. Treatment of diarrhea is based largely on these fundamental facts. First, deficits of water and electrolyte of this magnitude must be replaced; second, expenditure of water and electrolyte of this magnitude must be covered; third, the disturbances accompanying deficits of water and electrolyte must be rapidly overcome; fourth, assimilation of food must be restored before starvation leads to death.

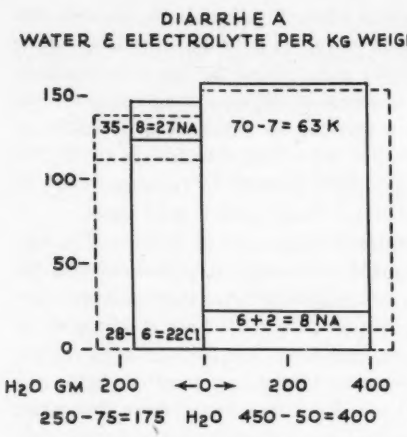

CHART 6. Diagram of probable state of body water and electrolytes in diarrhea produced by losses indicated in chart 2. Areas to left of 0 represent extracellular water and those to right intracellular water, both in terms of 1 kg. of normally hydrated body weight. Solid areas indicate state during dehydration while dotted lines indicate state of normal infant. Height of extracellular area represents concentration of Na/kg. water while height of intracellular area represents concentration of K. Amounts of water and electrolytes during dehydration are indicated by estimated normal contents minus losses.

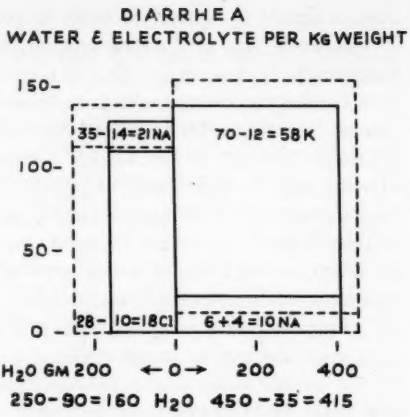

CHART 7. Diagram of probable state of body water resulting from diarrhea with heat stress inducing large volumes of sweat with losses like those of chart 3. Construction of diagram is similar to that of chart 6.

It has long been recognized that the acute disturbance in diarrhea which has been called alimentary intoxication is dependent chiefly on the losses of body water and electrolyte. From a modern point of view shock would be a better term than intoxication. Shock may be considered to be a state of tissue anoxia brought about by a discrepancy between blood volume and the capillary bed. The fall in blood pressure, oliguria, acidosis and changes in consciousness result chiefly from inadequate peripheral circulation and diminished extracellular fluids. In alimentary intoxication, shock is indicated by the cold extremities, grey pallor and cyanosis and the disturbances in consciousness. At Marriott's clinic, Utheim[7] showed that the circulation in the arm may be only one tenth of the normal. Loss of plasma water has long been considered the explanation of the high concentration of protein in plasma and red cells in blood. Over 25 years ago, Buckman and I[8] found that the plasma volume in diarrheal dehydration is about two thirds of the normal value. Recently Kerpel-Fronius[9] showed that the oxygen saturation of blood in the saggital sinus is greatly reduced. The extent of the reduction in venous saturation was correlated with the changes in consciousness. Calcagno and Rubin[10] found that the rate of glomerular filtration is sufficiently reduced to explain the rise in nonprotein nitrogen and the failure to regulate acid-base equilibrium. Replacement of sodium chloride and water rapidly restores the rate of glomerular filtration and provides the constituents for regulating extracellular fluids. Experimental studies in shock[11] indicate that permanent renal damage results when renal anoxia persists for several hours. The evidence of liver damage may also arise in a similar manner since the liver receives about 70% of its oxygen from portal blood and is, therefore, especially susceptible to reduction in the saturation of venous blood.[12] These changes in the function of the brain, liver, kidney

and other tissues become irreversible if shock persists too long. For this reason shock must be considered a medical emergency demanding immediate therapy restoring the circulation as rapidly as possible. Experimental work[13] indicates that shock due to deficits of extracellular electrolytes is most effectively treated by restoring the deficits of water, sodium and chloride. However, blood makes this form of therapy definitely more effective.

From clinical experience, Powers[14] showed that transfusions should be used in severe diarrheal dehydration as soon as the administration of electrolytes has improved the circulation. He emphasized that transfusions should be given promptly since it is impossible to recognize which patients will require this therapy in addition to salt solutions. He recommended fairly large transfusions (20 to 30 cc./kg.) which is in keeping with recent trends in the treatment of shock. Concentration of hemoglobin is not a contraindication to transfusions since the high hemoglobin is a result of shock and citrated blood does not increase the concentration. Evidence of anemia is not sought before using transfusions in severe diarrheal dehydration except as an additional indication.

Since the studies of Schloss and Stetson[15] and Howland and Marriott,[16] acidosis has been recognized as an almost constant feature of severe alimentary intoxication. These investigators used sodium bicarbonate to treat the acidosis but admitted that the early evidences of improvement were not followed by a decrease in mortality. Nevertheless rapid restoration of serum bicarbonate concentration has been emphasized as almost the most important phase of early treatment in many clinics. For this reason the effect of large doses of sodium bicarbonate in acidosis must be considered in the light of our present knowledge of distribution of water and electrolyte between extracellular and intracellular fluids.

Hartmann and associates[17] showed that the amount of sodium bicarbonate or lactate necessary to restore the concentration of bicarbonate in serum is greater than the amount of sodium bicarbonate present in extracellular fluids. It is about the same as the relative deficit of sodium in extracellular fluids plus the estimated normal intracellular sodium.[1] The studies of the serum electrolyte pattern in alimentary intoxication[18, 19] show that the decrease in serum bicarbonate is dependent on relative excess of chloride over sodium or relative deficit of sodium in relation to chloride in extracellular fluids. As was mentioned previously the relative decrease in sodium in extracellular fluids is dependent on transfer of sodium to intracellular fluids and not on greater deficits of sodium than chloride in the body. The retentions of equivalent amounts of sodium and chloride during recovery are only compatible with the serum concentrations during dehydration if high intracellular sodium is present at the beginning of treatment. Since large amounts of sodium in excess of chloride cannot be retained in extracellular fluids without producing alkalosis, considerable sodium must enter the cells when sodium bicarbonate is given in large amounts to patients with diarrheal dehydration. Chart 8 shows the intracellular retentions of Na and K during the period of fasting in the treatment of diarrhea when only sodium and chloride are given and when potassium in addition to sodium and chloride are administered. The two groups of cases show essentially the same retentions of cations but only sodium is retained in the cells when no potassium is available and potassium accounts for most of the cation retention when this ion is administered. Elkinton, Squires and Singer[20] showed that practically all the administered sodium bicarbonate given to cases of acidosis may enter the cells. Thus, while sodium bicarbonate undoubtedly hastens the restoration of the concentration of bicarbonate in extracellular fluids, it

probably interferes with the recovery of normal intracellular electrolyte if large amounts are given and no potassium is administered. In addition the failure to provide potassium increases the likelihood of alkalosis developing during replacement of extracellular electrolyte. This conclusion is indicated by the finding that deficit of potassium leads to alkalosis if renal adjustment is achieved in the presence of abundant sodium chloride and water.[21] Serum potassium concentration also becomes very low under these circum-

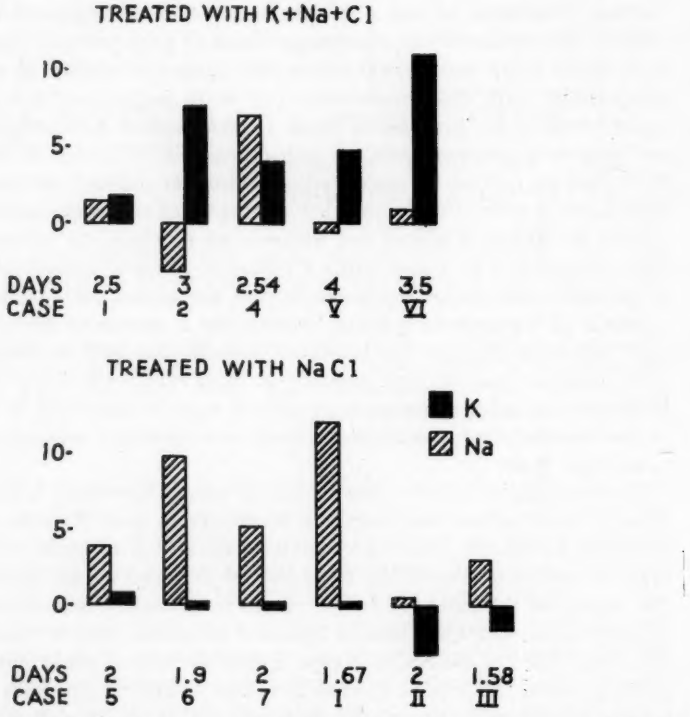

CHART 8. Balances of Na and K in intracellular fluids during period of treatment when milk feeding was omitted. One group was treated parenterally and orally with fluids containing K, Na and Cl while others received only Na and Cl. Balances are expressed in mM/kg. body weight.

stances and further losses of this ion develop. For this reason the treatment of acidosis should provide potassium as well as appropriate amounts of water, sodium and chloride.

If all the intracellular deficits of potassium could be readily restored and lead to rapid release of intracellular sodium, probably the acidosis of diarrhea would be corrected by replacement of body water and potassium together with enough sodium chloride to restore the volume and concentration of extracellular fluids. Large deficits of potassium in rat muscle can be rapidly restored if large amounts of potassium chloride are given.[22] However, the abnormally high intracellular sodium only returns to normal after 3 or 4 days. The restoration of intracellular potassium in patients is apparently a slow process requiring 4 to 6 days for large deficits.[23] While cellular composition is being restored, intracellular sodium may not become immediately available to extracellular fluids or intra-

cellular sodium may even increase. For these reasons extracellular fluids should be expanded with a fluid containing sodium and chloride in about the same relative amounts as is found in normal extracellular fluids together with an amount of potassium that will cover continuing losses and provide sufficient amounts of this ion for intracellular retentions without danger of potassium intoxication.

During treatment of patients with diarrhea by these principles, the concentrations of bicarbonate in serum are partially restored within 24 hours and almost invariably reach essentially normal levels in 48 hours even in the most severe cases of acidosis.[24] Alkalosis does not develop and the concentrations of potassium remain between 4 and 7 mM/l. The fully developed picture of the postacidotic state described by Rapoport and associates[25] has not been encountered although low calcium tetany has been seen once or twice. The patients look well after the initial therapy despite persistent mild to moderate acidosis. Since the dangers of alkalosis and low serum potassium are avoided, it is advantageous to permit acidosis to recover more slowly than when large amounts of sodium bicarbonate are administered.

A period of fasting has been one of the chief therapeutic measures used in diarrhea in the past; it was considered essential by the German school; it was especially emphasized in the *regime de l'eau pure* by Marfan[26] and good results were obtained by Monrad[27] using quite long periods of fasting. With modern fluid therapy, some investigators have questioned its necessity. Chung and Viscorova[28] found no prolongation of the period of serious diarrhea when parenteral fluid therapy was continued during early feeding. However, these investigators found that the stool volume was increased by milk feeding but regarded this untoward effect as not necessarily harmful since more water and electrolyte were absorbed than when only water was given by mouth. They contend that milk feeding does not produce intolerance to food but merely makes manifest the intolerance that is already present. These observations must be weighed against the clinical experience on which fasting is established.

Finkelstein[29] based the period of fasting on the appearance of a clinical picture which he called "alimentary intoxication" because the symptoms appeared with or were aggravated by milk feedings. In response to food, certain infants lose weight, look sick, develop fever and are likely to vomit. Diarrhea may be aggravated or develop if not already present. These events occur in some normal infants in response to infections or hot weather. Infants who are undernourished owing to repeated infections or inappropriate foods are especially likely to show this reaction. The disturbance improves when food is omitted and only water is given by mouth. Small amounts of food may be tolerated when large amounts produce an adverse reaction. By giving less food than that which induces "alimentary intoxication" sufficient recovery takes place eventually to permit adequate food intake. From the point of view of the relation to nutrition, Finkelstein classified the stages of the reaction into (1) dystrophy when some difficulty is encountered in giving enough food to restore nutrition, (2) atrophy when considerable difficulty is encountered and (3) "decomposition" when the infants seem unable to take enough food to recover.

Loss or instability of body water was considered an essential feature of alimentary intoxication. The loss of body water was explained in some cases by vomiting and diarrhea but in others, Finkelstein postulated a disturbance in the ability of the tissues to "bind water." The phenomena have not received much attention recently in America and need interpretation in the light of modern knowledge of tissue water and electrolyte.

Loss of weight and sickness may be readily produced in premature infants by feeding protein milk.[30] Balances show retention of chloride without sodium leading to acidosis. No diarrhea or vomiting explains these disturbances in water and electrolyte metabolism. Some infants who are not suffering from diarrhea fail to thrive on ordinary milk mixtures.[31] These infants show acidosis and recover when the disturbance in acid-base equilibrium is corrected. The administration of protein foods with insufficient water readily produces the same phenomena in infants and puppies.[32, 33] The phenomena can be explained by some difficulty in maintaining body water and electrolyte with certain renal excretory loads. Losses of electrolyte in the stools aggravate this difficulty since the kidneys must compensate for the abnormal losses in the stools. For this reason stabilization of body water and electrolyte is attained with difficulty as long as food greatly increases the losses of water and electrolyte in the stools.

Hesitation to use fasting to facilitate the recovery from dehydration can hardly arise from any doubt as to the validity of the observations that milk feeding increases the water and electrolyte in the stools and that infant's kidneys have difficulty in regulating body water and electrolytes when required to excrete certain loads of electrolytes. Absorption of more water and electrolyte may not make the internal adjustments easier since the kidneys must adjust to an abnormal load if stools are voluminous. The hesitation in using fasting in diarrhea arises from the fact that undernutrition is one of the most dangerous features of diarrhea and this fact may make it desirable to prevent aggravation of undernutrition at the risk of greater difficulty in restoring body water and electrolytes.

Before instituting our present therapeutic regime, fasting often seemed to be associated with undesirable consequences. While all fluids were given parenterally and contained no potassium, the infants frequently looked pale, sick and weak. Sometimes they seemed unable to continue to maintain the marked improvement usually manifest after 24 hours. Weight might be maintained or edema develop while serum chloride and bicarbonate concentrations became normal. However, a considerable number collapsed on the third or fourth day whether or not food was started. With the present regime which administers a mixture of glucose, Na, K and Cl orally and parenterally during the period of fasting, the infants almost invariably look well, their skin becomes pink, and they take prescribed amounts of oral fluids without vomiting. When the stools and general condition indicate that fasting is no longer indicated, food is almost invariably taken without adverse reaction. These results have made me believe that a large part of what seemed to be an adverse reaction to fasting is dependent on omission of potassium during this period. This conclusion is supported by the fact that a normal subject develops deficits of potassium on a regime giving only glucose and sodium chloride.[34]

Nevertheless we have encountered some infants who have continued to have watery stools leading to dehydration after periods of fasting as long as 4 or 5 days which seems to be as prolonged a period as is likely to be beneficial. Food has continued to produce serious diarrhea for 2 to 3 months in several infants and for 6 months in two. Fasting decreased the diarrhea but obviously could not be prolonged indefinitely nor be repeated often. Eventually the patients recovered on a regime providing a milk mixture containing 80 to 100 calories in 150 cc. fluid/kg. body weight/day. This intake had to be supplemented occasionally by clyses of Na Cl, KCl, and Na lactate and infusions of glucose.

In a majority of the patients a change in the type of food made no obvious difference but in at least three there was unmistakable evidence of an adverse reaction to cow's milk—probably an allergic reaction since it did not occur on a mixture of amino acids, fat and

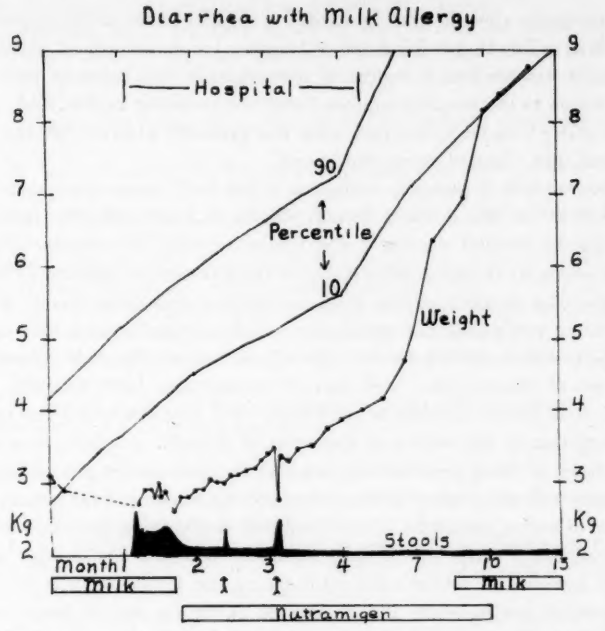

CHART 9. Weight curve of infant suffering from severe diarrhea complicated by allergic reaction to cow's milk producing severe diarrhea. Stewart's percentiles are indicated. Note change in time scale at 4 mo. One bottle of milk is indicated in period of nutramigen® feeding by arrow. No loss of weight was demonstrated after first bottle because infant received clysis before weighing.

carbohydrates. The following patient became so sick and developed such severe diarrhea when fed milk that omission of the usual types of food was essential for recovery. I am indebted to Drs. Powers and Cooke who made the crucial changes leading to recovery.

The patient was born weighing 3100 gm. Since the mother was not married, he was transferred to an orphan asylum on the seventh day weighing 2900 gm. He did not thrive in this institution since he was admitted to the hospital on his 31st day of life weighing 2720 gm. He had had diarrhea for 2 days leading to dehydration and acidosis (Cl, 119 and CO_2 15 mM/l.). He responded to parenteral fluid therapy but continued to have diarrhea when fed. On the 8th day of treatment and the 5th day after milk was started, he was again fasted for 24 hours because of dehydration. He again responded to milk feeding with such severe diarrhea that recovery seemed impossible. He presented the picture which Finkelstein called "decomposition." He was again given parenteral fluids, 1 cc. of Upjohns lipo extract of the adrenal cortex twice daily and changed to a food containing amino acids, fat and carbohydrate (Mead Johnson, nutramigen®). Within 24 hours, the response was so favorable that recovery seemed likely. At this time it was not clear whether the favorable response was due to cortical extract or omission of milk. On the 38th day in the hospital (78th day of life) he again became sick from diarrhea following one bottle of milk. On the 93rd day of life he again received one bottle of milk by mistake. This time he vomited within two hours and developed such severe diarrhea that the weight decreased from 3480 to 2840 gm. within 18 hours. Although gain in

weight was unusually slow, he was discharged to a foster home on the 132nd day of life.

I am indebted to Dr. Martin Randolph of Danbury for the subsequent observations. The infant gradually recovered on a regime of nutramigen®. His behavior which suggested mental retardation in the hospital improved with the return of health. After finding that one drop of milk produced no reaction, milk was gradually added to his diet and he now takes the usual diet. Chart 9 shows the course.

The reaction to milk is probably analogous to but much more severe than the one described by Rubin[35] in the newborn period. We do not know that the failure to thrive before entering the hospital was due to this type of reaction. It is possible that sensitivity was acquired owing to increased permeability of the intestines to proteins during diarrhea. Similar observations in other infants make us feel sure that some infants with diarrhea cannot recover on cow's milk but apparently can take a nonallergenic food satisfactorily. We do not believe the evidence for this type of reaction is sufficiently frequent to justify the routine use of nonallergenic milk during convalescence from diarrhea. However, a nonallergenic milk should certainly be used when milk produces an adverse reaction.

Finally inspection of the outline of treatment of infantile diarrhea can serve to recall the various phases of therapy and the discussion of the basis for the procedures. The actual details will vary with the severity of the illness and the reaction of the patient.[24] I believe the therapy of diarrhea should be directed without emphasizing any one phase of treatment. The treatment of shock with blood transfusions as well as replacement of water and electrolytes is essential in severe cases. Minimizing the losses of water and electrolyte through a period of fasting seems almost essential during the first 24 hours and certainly make stabilization of body water and electrolyte much easier as long as milk increases the stool volumes greatly. Administration of water, Na, Cl and K for replacement is essential for recovery. Although most patients will restore body potassium when they can take food, parenteral and oral potassium is safe and is indicated as long as food is not taken in adequate amounts. Normal acid-base equilibrium is satisfactorily attained without special doses of sodium bicarbonate. Occasionally infants must be fed when milk produces large stool volumes. Parenteral therapy must then supplement oral feeding. Some infants have an allergic reaction to milk which makes recovery on milk practically impossible. The use of nonallergenic milk has been successful in these cases.

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TETANY AND PARATHYROID HYPERPLASIA IN THE NEWBORN INFANT: INFLUENCE OF DIETARY PHOSPHATE LOAD

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EARLY workers[1,2] noted that cow's milk, particularly whey, had a tetanogenic action in young rachitic infants. In 1921 the high phosphate content of cow's milk whey was identified as a major factor which aggravated rachitic tetany in older infants.[3] Bakwin suggested in 1937 that the high phosphate content of cow's milk might be one of the etiologic factors in tetany of the newborn infant,[4] an hypothesis which has received recent support.[5,6] Tetany of the newborn infant as a clinical syndrome has been repeatedly described, and the literature thoroughly reviewed elsewhere.[7] The present communication presents observations relating to the influences of excess P intake on the metabolism of newborn infants. The material will be divided into the following categories: (1) correlation of high P intake with manifestations of neonatal tetany (presentation of three cases), (2) description of the evidences of excess dietary P in newborn infants who did not show typical tetany (presentation of three cases) and (3) tabulation of data correlating dietary history with parathyroid histology in 16 newborn and five older infants.

METHOD

Methods for the chemical procedures used in this study have been described in a previous publication from this laboratory.[8] The term "ionized Ca" as used refers to a value calculated from total serum Ca and total serum protein by the nomogram of McLean and Hastings.[9]

1. Relationship Between Dietary P Load, Ca/P Ratio, and Manifestations of Neonatal Tetany

Case 1. R. B. was a 6 day old boy who had exhibited tetany 1 day prior to entry. The infant was born of an uneventful pregnancy and labor. Breast milk alone had been offered the 1st 2 days of life. Then an evaporated milk, water and corn syrup formula of unknown proportions was substituted, which the infant took "vigorously" for the next 3 days. At 3 a.m. on the 6th day of life tetanic twitching of the face and extremities began, originating on the right side each time. These signs continued throughout the day until the infant was brought to the hospital. Physical examination was negative save for occasional twitches. Subdural tap was negative. Temperature was normal. Treatment with $CaCl_2$, 2 gm./24 hr. was begun, added to a formula composed of cow's milk, water and corn syrup. After 2 days the $CaCl_2$ was replaced by Ca lactate, 3 gm./24 hr. No tetanic episode occurred after treatment was begun.

Chart 1 shows the serum values for ionized Ca and inorganic P obtained on entry and subsequent to treatment with oral Ca salts. The lower portion of the chart shows the Ca/P ratio of the infant's diet.

Case 2. L. R. was a 9 day old girl who had suffered 10 episodes of "stiffening out" with clenched

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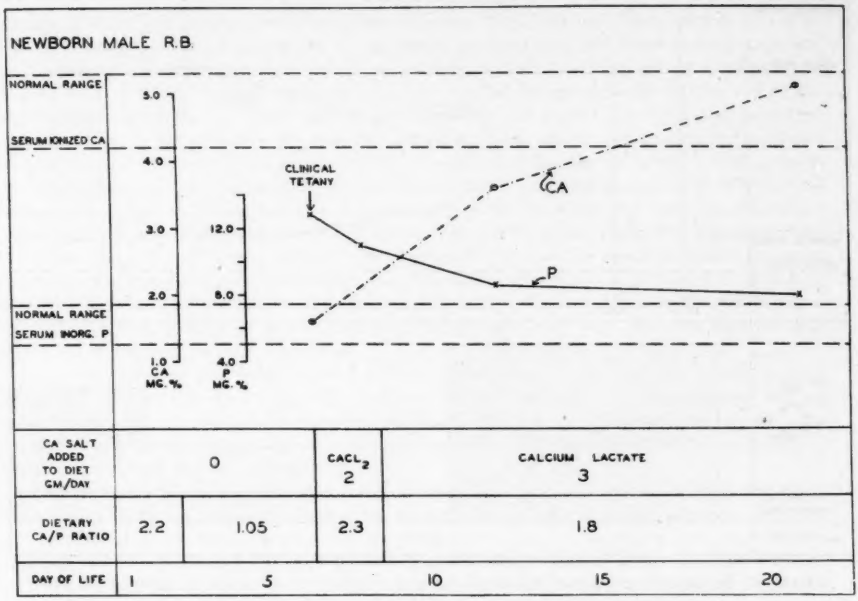

CHART 1. Serum concentrations of ionized Ca and inorganic P plotted with reference to added dietary Ca and dietary Ca/P ratio in newborn infant with tetany.

fists during the 24 hr. prior to entry. Shortly after birth feedings of an evaporated milk formula were begun, but at the age of 2 days were changed to a commercial powdered cow's milk formula. The infant "ate well" and had no vomiting or fever. On the 9th day of life the signs described above led to hospital admission. Shortly after entry there were 2 episodes, lasting 1 to 2 min., of generalized left-sided twitching. Reflexes were generally hyperactive. Lumbar puncture and subdural taps were negative. There was no fever.

Chart 2 shows the concentration of P in the feedings ingested by the infant prior to tetany and during its hospital stay, together with serum ionized Ca and inorganic P values. The transverse dotted line in the bottom portion of the figure contrasts the low P concentration in human milk with the high P concentration of the cow's milk formula in this case. For therapy, P-free feedings were given for 3 days, with very dilute milk feedings for a period thereafter. No further twitching occurred, and serum ionized Ca and serum inorganic P returned toward normal.

Case 3. B. D. was a 7 day old boy who entered the hospital because of twitching and cyanosis 1 hr. previously. Delivery was normal. A commercial dried cow's milk preparation was begun on the third day of life, and was taken well. The concentration of P in this formula is the same as that shown in chart 2. On the 7th day edema of the face and eyelids was noted, followed by the signs described above. Physical examination was noteworthy in that there was moderate edema of the face. There was no fever. Serum values were: Na 150 mEq./l., Cl 107 mEq./l., mg. 0.95 mEq./l., Ca 6.2 mg./100 cc., inorganic P 8.8 mg./100 cc., total protein 5.5 gm./100 cc., ionized Ca 3.0 mg./100 cc. With added dietary Ca no further twitching occurred and there was a fall of serum inorganic P and a rise of serum Ca values. Ten days after admission serum ionized Ca was 5.0 mg./100 cc.

2. Newborn Infants Without Typical Tetany Showing Other Evidences of Excess Dietary Phosphate

Case 4. B. L., a 3 day old boy, was transferred to the Massachusetts General Hospital because of cyanosis and a convulsion. After a full term, normal delivery the baby was immediately started on a

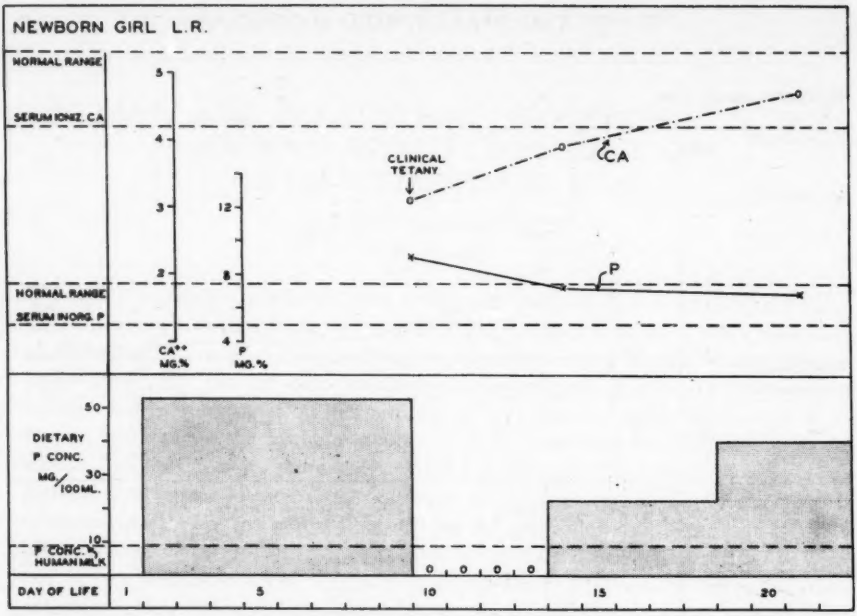

CHART 2. Serum concentrations of ionized Ca and inorganic P in newborn infant with tetany. Lower portion of chart contrasts P concentration of diet ingested by this infant with P concentration of human milk.

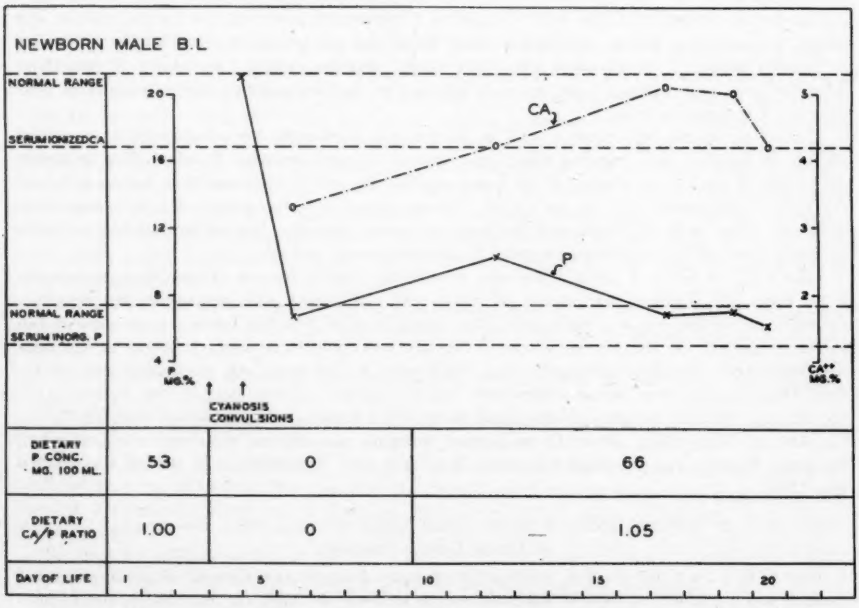

CHART 3. Serum concentrations of ionized Ca and P together with dietary P concentration and dietary Ca/P ratio in newborn with cyanosis and convulsions.

commercial dried cow's milk formula in another hospital. The infant took 60 cc. of this each 4 hr. without difficulty for the 1st 2 days. On the day before entry the baby was noted to be irritable and had a tremor of its extremities. Early on the day of entry the baby had a generalized convulsion and "turned black all over." Oxygen was given and there was improvement shortly. For the rest of the day the baby was unable or unwilling to take its formula, and from 7 a.m. to 3 p.m. passed no urine or stools. In the afternoon the baby "turned black" again and so was brought to the Massachusetts General Hospital. Physical examination revealed a weak, afebrile newborn with a feeble cry. While being admitted he suddenly turned deeply cyanotic and respirations ceased. When placed in oxygen he began to breathe again, with tremulous motions of tongue and lips. There was slight cyanosis even at rest, with spells of apnea. The Chvostek and Trousseau signs were negative and the Moro was sluggish. All tendon reflexes were depressed. The muscles appeared flabby, peripheral circulation was poor, and there was bradycardia. The infant was placed on parenteral fluid therapy together with penicillin, sulfadiazine and streptomycin. Stool and spinal fluid cultures were negative. One blood culture flask grew out staphylococcus albus, and there were moderate staphylococcus aureus and rare escherichia coli in the throat.

On admission there was found a blood glucose concentration of 126 mg./100 cc. and a serum inorganic P concentration of 21 mg./100 cc. (determined in duplicate). At that time there was not enough serum for a serum Ca determination, but on the next day total serum Ca was 6.4 mg./100 cc., total serum protein 4.9 gm./100 cc. and serum ionized Ca 3.2 mg./100 cc. WBC count was 5.2 thousand/cmm. with Hgb 19.5 gm./100 cc.

Chart 3 shows the concentrations of serum inorganic P during the hospital stay of this infant. There was a sharp fall to 6.7 mg./100 cc. on the 2nd hospital day following parenteral hydration and withdrawal of the high P feeding. On the 9th hospital day, 3 days after a cow's milk formula (2 parts water: 1 part milk) had been started, there was another rise of serum inorganic P to 10.3 mg./100 cc. (determined in duplicate). The 2:1 milk and water mixture was continued and by the 17th hospital day both Ca and P values were normal.

Case 5.* J. C. was placed on a cow's milk formula of unknown dilution on the 3rd day of life. On the 7th day the infant had generalized convulsions with cyanosis and died. Autopsy revealed an imperforate anus and bronchopneumonia. No blood chemical determinations are available. Figure 1A shows a section from the hyperplastic parathyroid gland of this newborn. No oxyphil cells can be seen, and the water-clear cells show cytoplasm that is distended, suggesting a relative scarcity of nuclei. This section may be contrasted with the normal-appearing, closely packed cells of the parathyroid in breast-fed newborns (Figs. 2A and B).

Case 6. E. P. was given a commercial dried cow's milk formula until the 9th hospital day when its temperature went to 39.4° C. There was an Esch. coli bacteremia. Edema of the legs, scrotum and penis occurred. The results of chemical determinations on the blood are not available, but figure 1B shows the hyperplastic nature of this patient's parathyroid glands, with greatly enlarged water-clear cells.

3. Correlation of Dietary History with Parathyroid Histology in Newborns

Table 1 records data on those newborn infants studied by Kaplan[10] in which both dietary and histologic data were available. Normal parathyroids were exhibited by 8 infants, all less than 24 days of age. Of this group, 4 had been fed nothing but human milk, one received human milk with a cow's milk supplement and 3 received no oral feedings. Hyperplastic parathyroid glands were found in 8 infants, all less than 22 days of age. Of these 7 had been fed cow's milk formulas and one received no oral feedings. Unfortunately, these 2 groups are not entirely comparable, since half the newborn infants with normal parathyroids were 28 hr. of age or less, whereas the youngest infant with parathyroid hyperplasia was 4 days old.

Five older cases, age 4 mo. to 10 7/12 yr., all showed normal parathyroid glands. Of these, one had been breast fed, 2 received cow's milk formulas and 2 had received both human and cow's milk.

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* The author is indebted to Dr. Sidney Farber, Pathology Department, Children's Hospital, Boston, who made available autopsy protocols and slides of parathyroid glands referred to in the latter cases discussed. These cases are from a series in which hyperplastic and normal newborn parathyroids were studied by Dr. Eugene Kaplan and described in detail elsewhere.[10]

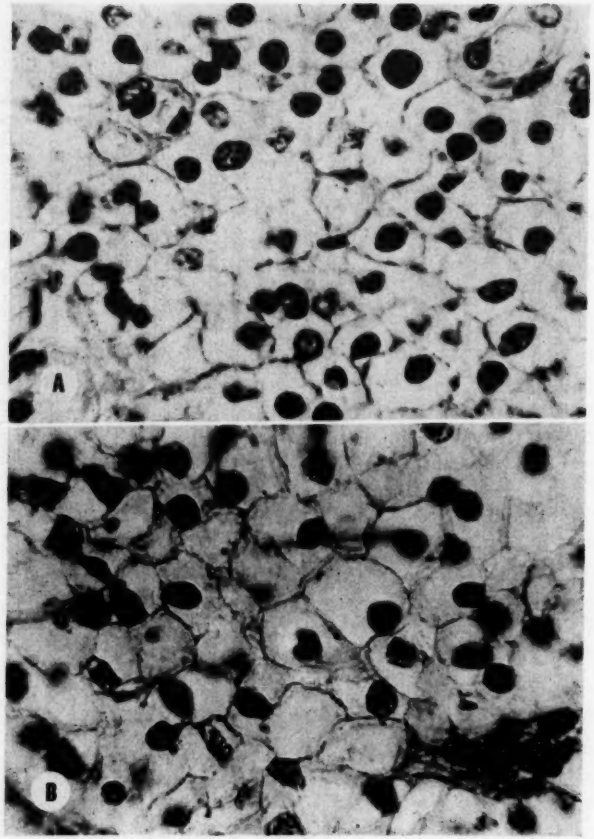

FIG. 1. Hyperplastic parathyroid glands from 2 cow's milk-fed newborns. Swelling of water-clear cells is shown in both 1A and 1B. (×453 as printed.)

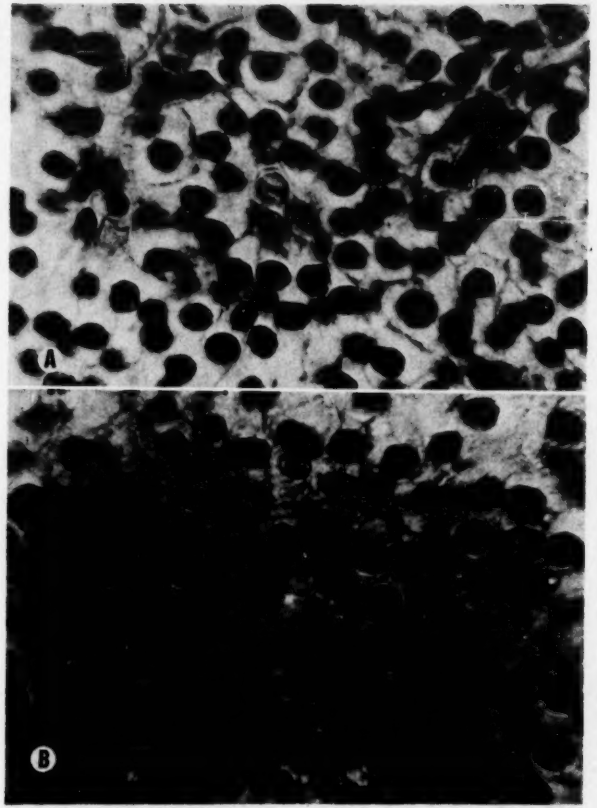

FIG. 2. Densely packed cells of parathyroid glands from 2 breast-fed newborns. (×453 as printed.)

In later infancy and childhood there appears to develop an increased ability to excrete large loads of phosphate. As growth progresses there is also a decrease in phosphate intake when expressed on a per square meter surface area basis. These 2 factors might make the development of parathyroid hyperplasia in the older child less likely. Although there are inconsistencies in the data presented, there is a suggestive relationship between cow's milk feeding in early infancy and parathyroid hyperplasia.

Discussion

In the cases presented the association of cow's milk feedings of relatively high P concentration and clinical tetany of the newborn infant is noteworthy. Case 6 evidenced no visible tetany but showed other manifestations of dietary P load. The last three cases together with the tabulated autopsy data would suggest that there may be other signs than clinical tetany per se, such as cyanosis, generalized convulsions, apnea and parathyroid hyperplasia, which may be the result of feedings of high P concentration. The latter findings emphasize the importance of a serum inorganic P determination in the differential diagnosis of neonatal distress.

There is good experimental evidence that excess dietary P in the face of limited kidney function may have profound effects both on parathyroid and renal tissue. Animal studies have shown that excess P administration may cause parathyroid hyperplasia,[11] and the histologic findings in Cases 5 and 6 would seem to bear this out. Renal lesions have been produced in animals by parenteral[12] and oral[13] high P intakes. The kidneys of the latter animals exhibited histologic lesions a month after cessation of the high P diet, perhaps indicating irreversible changes.

Crawford and colleagues found that animals with limited or absent parathyroid function (parathyroidectomized) showed a lack of ability to maintain a constant serum P concentration by adjustments in renal P clearance when given excess dietary P.[14] McCrory and colleagues found that newborn infants who showed elevated serum inorganic P concentration with or without tetany had reductions in inulin clearance.[15] Both normal newborns and newborns with tetany have been found to respond to the administration of 15 to 20 units of parathyroid extract with an increase of urinary P excretion.[15,16] The parathyroid hyperplasia which has been described would appear to be compensatory, due to hyperphosphatemia, although insufficient to cause a fall in serum P concentration. This confusing phenomenon has been aptly described by McCrory and Barnett as "inadequate compensatory hyperplasia."[17]

Insofar as causation of tetany of the newborn infant is concerned, excess P intake appears to be an important, but not exclusive, factor. That there are unexplained aspects is indicated by the occasional occurrence of this syndrome in breast-fed infants and by Bakwin's failure to produce tetany in newborn infants with oral phosphate solution, although he did produce extreme hyperphosphatemia and hypocalcemia.[4]

Hyperfunctioning of the maternal parathyroid gland may predispose the young infant to tetany.[18] This possibility should be suspected in cases of newborn tetany fed breast milk, and in persistent tetany in a newborn.

Several workers have demonstrated an excess of estrogens in the blood and urine of newborn infants for the first few days of life,[19-21] and the influence of estrogenic compounds on increasing blood Ca concentration is well authenticated.[22, 23] Crawford administered 1.67 mg. of estradiol dibenzoate daily for 11 days to a newborn mongoloid idiot. The infant was fed an evaporated milk formula, and the injections were begun on the

TABLE 1

DIETARY AND AUTOPSY DATA ON 16 NEWBORN INFANTS AND 5 OLDER INFANTS CORRELATING NEONATAL PARATHYROID HYPERPLASIA WITH INGESTION OF HIGH P FEEDINGS

A. Less than 22 days old
(Hyperplasia)

Autopsy No. (Boston Children's Hospital)	Sex	Col.	Age (days)	Feeding	Stated Cause of Death	Degree Parathyroid Hyperplasia
A-32-132	F	W	4 d.	CM	(a) Congenital heart (b) Bilateral choanal atresia	+++
A-39-63	F	W	6 d.	0 Parenteral therapy only	(a) Intestinal obstruction (b) Peritonitis	++++
A-39-74	F	W	5 d.	CM	Atresia of intestine and duodenum	+++
A-39-46	F	—	7 d.	EM and Karo	(a) Septicemia, E. coli (b) Prematurity, B.W. 1.7 kg.	+++
A-37-8	F	W	8 d.	CM	(a) Imperforate anus (b) Bronchopneumonia	+++
A-39-49	M	W	10 d.	Olac	(a) Intracranial hemorrhage (b) Prematurity, B.W. 1.7 kg. (c) Edema	++++
A-34-11	F	W	17 d.	EM and Karo	(a) Bronchopneumonia (b) Prematurity, B.W. 2.0 kg.	++++
A-34-77	M	W	21 d.	CM	(a) Septicemia (staph.) (b) Pneumonia (c) Peritonitis	+++

21st day of life. There appeared to be an increase of serum inorganic P following withdrawal of the estradiol.[24]

Harrison has recently obtained data which demonstrate that infection may play a role in affecting the metabolism of serum inorganic P. This worker found that a group of children with severe infections such as meningitis, septicemia and empyema had low serum inorganic P concentrations.[25] The serum values returned to normal when the infections subsided. During these studies there were no known significant changes in the dietary intake of Ca, P or vitamin D. The foregoing data should be borne in mind when reviewing table 1, since a number of the newborn infants therein described suffered from infections.

The observation of Harrison and colleagues[26] that a patient having both hypokalemia

TABLE 1—(*Continued*)

B. Less than 24 days old
Normal Parathyroids

Autopsy No. (Boston Children's Hospital)	Sex	Col.	Age	Feeding	Stated Cause of Death	Degree of Parathyroid Hyperplasia
A-31-100	F	W	4 hr.	0	(a) Prematurity (b) Petechial hemorrhage in viscera	0
A-30-22	M	W	28 hr.	BM	(a) Atelectasis (b) Prematurity, B.W. 0.6 kg.	0
A-39-135	M	W	8 hr.	0	(a) Prematurity, B.W. 0.9 kg. (b) Subarachnoid hemorrhage	0
A-40-132	M	W	1 day	BM	(a) Interstitial pneumonia (b) Pulmonary congestion	0
A-40-164	M	W	4 days	0	Imperforate anus	0
A-38-127	F	—	7 days	Mixed CM and BM	(a) Full term (b) Intestinal atresia	0
A-33-154	F	W	21 days	BM	Myocarditis	0
A-38-68	M	W	23 days	BM	(a) Prematurity (b) Staph. aureus septicemia	0

and hypocalcemia did not evidence the tetany that would have been expected from low serum Ca may help explain why some newborn infants with hypocalcemia get tetany and some do not. Engel and colleagues have amplified this work[27] and found that hypocalcemic tetany in adults was accentuated by the intravenous infusion of KCl. This effect was abolished by the administration of Ca salts. It is of interest that Klercker and Odin in 1925 observed that the intravenous infusion of potassium phosphate solutions produced increased electric irritability more readily than equivalent amounts of sodium phosphate solutions,[28] and that the appearance of hyperirritability during potassium phosphate infusion did not always correlate with lowering of the serum Ca concentration. Further studies of serum Na, K and Ca relationships in normal newborns and in newborns with tetany are in order.

SUMMARY

Three cases of newborn tetany are described, pointing out the relationship between dietary phosphate load and the manifestations of this disease.

An additional three newborn infants are described who showed other symptomatology than tetany in association with dietary phosphate load.

TABLE 1—(*Continued*)

C. Age 4 mo. to 10 7/12 yr.
Normal Parathyroids

Autopsy No. (Boston Children's Hospital)	Sex	Col.	Age	Feeding	Stated Cause of Death	Degree of Parathyroid Hyperplasia
A-38-126	F	—	4 mo.	BM+CM	(a) Equine encephalitis (b) Bronchopneumonia	0
A-32-168	M	W	6 mo.	BM+ Lactogen	Hydrocephalus	0
A-40-116	F	—	2 3/12 yr.	CM	Enteritis	0
A-38-89	F	—	5 3/12 yr.	BM 1st 9 mo. Then CM	(a) H. influenzae meningitis (b) Bronchopneumonia	0
A-38-156	—	—	10 7/12 yr.	CM	Medulloblastoma	0

Legend: BM is breast milk
CM is cow's milk formula
EM is evaporated milk formula

Data concerning diet, cause of death and degree of parathyroid hyperplasia are tabulated in eight newborns who were found to have parathyroid hyperplasia at autopsy. Similar data are tabulated on eight newborns and five older children who were found to have normal parathyroid glands at autopsy.

Several other factors possibly involved in newborn tetany and newborn parathyroid hyperplasia are discussed. The importance of measuring serum inorganic P in the differential diagnosis of neonatal distress is pointed out.

Acknowledgments

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SPANISH ABSTRACT

Tetania e Hiperplasia de las Paratiroides en el Recién Nacido

Se describen 3 casos de tetania del recién nacido, haciendo notar la relación entre el exceso de fosfatos en la dieta (por la leche de vaca) y las manifestaciones de esta enfermedad. Se presenta otro recién nacido que no tuvo tetania, pero en el cual hubo hiperfosfatemia, apnea y cianosis, asociadas con una alimentación alta en fósforo. En 8 recién nacidos que tuvieron a la autopsia hiperplasia de la paratiroides, se tabularon los datos concernientes a la dieta, causa de muerte y grado de hiperplasia de dichas glándulas. Estos mismos puntos fueron analizados en 8 recién nacidos y en 5 niños mayores que al examen post mortem tuvieron paratiroides normales. Los hallazgos sugieren que hay una relación entre la alimentación con leche de vaca en el recién nacido y la hiperplasia de las paratiroides. No se demostró esta relación en niños mayores.

Se recomienda el estudio del fósforo inorgánico en el plasma de aquellos recién nacidos, alimentados con leche de vaca, que se encuentran en situación precaria sin una causa satisfactoria que la explique.

The Johns Hopkins Hospital

INFECTIVE GANGRENE OF THE MOUTH
(Cancrum Oris)

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Ibadan, Nigeria

ECOLOGIC BACKGROUND

THE Yoruba are the predominant people of Western Nigeria, their territory extending from the river Niger in the North to the Lagos lagoon in the South, the Dahomey frontier in the East and the Benin country in the West. Ibadan, the principal city of Yorubaland, has a population of over half a million. It lies at the edge of the coastal forest plain and is the centre of the cocoa-growing area of Nigeria. The city itself is a sprawling accumulation of unhygienic tin-roofed mudbrick buildings and has been the site of a considerable African settlement for over a hundred years.

The Yoruba people of Ibadan are, for the most part, peasant farmers and petty traders. Their diet is mainly vegetarian, the chief farinaceous foods being yams, cassava and maize. Animal protein is deficient in the food of the majority, as cattle cannot be reared locally. Fresh milk is unobtainable and little game is to be found, although rabbits and bushrats are hunted with primitive muzzle-loading guns. Fortunately, palm oil is abundant and is used universally in the vegetable stew that forms the nucleus of most Yoruba meals.

Yoruba children continue to be breast-fed for from one to three years. At the end of this period, they are fully weaned onto a diet made up almost exclusively of carbohydrate and water. "Pap," here a gruel-like paste of maize and water, is the principal food. Milk plays no part in infant feeding, being either not obtainable or prohibitively expensive.

CLINICAL CLASSIFICATION

In many tropical countries, especially during early childhood, various gangrenous lesions of the mouth and face have been described. These have usually been considered together under the term "cancrum oris." As to the present series, it is felt that this term is not precise enough as it implies a gangrenous destruction of soft tissues, which was not alway found. The term "infective gangrene of the mouth" is used here, because it is felt that it is rightly noncommittal in view of the uncertainty as to real causes of the disease.

Clinically, the cases of infective gangrene of the mouth reported on here fall into two groups: Stage I, showing only gingivitis and infective necrosis of bone, and Stage II, showing gingivitis, bone necrosis together with a varying degree of gangrene of the soft tissue of the oral cavity.

CLINICAL DESCRIPTION

In this group there were 53 Yoruba children of poor parents. They were admitted to hospital between January 1949 and May 1951. Their ages varied from 2 to 5 years, the usual age of onset being about 3 years. All had had a diet unquestionably deficient in

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protein for a period varying from 6 months to 2 years. No history of any specific fever was elicited. Most commonly the mothers reported that there had been foetor oris and increased salivation for 1 to 2 weeks. This was followed by swelling of the mouth, fever and ulceration of the gum margin. Frequent stools and cough were early symptoms in about half the patients.

Examination in Stage I showed a tender, firm swelling of the affected part of the maxilla or mandible, varying from a few centimetres in length to a huge mass involving the whole of the affected bone. Gingivitis and marked foetor oris were invariably present. Externally, there was usually swelling of the overlying part of the face, often with actual oedema. The superficial appearance in some early cases resembled that seen in infantile cortical hyperostosis,[1] although the history, clinical examination and radiologic appearance were quite dissimilar.

Quite early, it was possible to see that several teeth near the centre of the infective mass had become loose and, in successfully treated cases, later dental extraction showed that infection had extended into bone substance, producing a sequestrum varying in size up to involvement of almost the whole maxilla or mandible. In about 50% of patients at Stage I, there was, in addition, superficial ulceration of the adjacent cheek. It is felt that these would probably have passed into Stage II if no treatment had been given.

Patients in Stage II were admitted with either fully developed gangrene or obviously incipient necrosis. Examination revealed extensive gingivitis and varying degrees of bone involvement, together with a definite lesion of the fleshy tissues of the face. In the earliest of these, infection was present on the inner surface of the cheek opposite the maximal area of bone involvement. The whole area both inside and outside the cheek, had a tense, livid, brawny, deep reddish appearance, which was always followed by actual gangrene, despite therapy.

The majority in Stage II presented at hospital with gangrene already developed. A clearcut line of demarcation could be seen, the blackened necrotic centre being surrounded by a yellowish leathery rim. After a few days, the gangrenous area became loosened and was slowly sloughed, leaving sometimes a huge cavity in the face. It was difficult even then to estimate the extent of the bony involvement, but this was usually greater than at first seemed apparent. In some cases, the sequestrum remained adherent for as long as a month, but, in all successfully treated cases, the bone was eventually removed by rocking and traction with forceps.

The general condition on admission varied, but most of these children were very ill, often apparently moribund. All were miserably malnourished. Mild clinical rickets, commonly seen in Ibadan,[2] was present in about 20%. Signs of deficiency of protein and the vitamin B complex were found in most cases. All had some degree of hepatosplenomegaly, but in such an hyperendemic malarial zone this cannot be regarded as particularly unusual.

A moderate or marked intermittent temperature was seen for the first few days, although the most toxic cases were afebrile. A moderate hypochromic anaemia and a slight polymorphonuclear leucocytosis was usual. Malarial parasites (*P. falciparum*) were identified in the blood of 60%. Although stool examinations showed multiple helminth infection in most patients, there was no relation to severe infection with the hookworm. The Kahn test was positive in only two children.

Results of Treatment

Intramuscular procaine penicillin 0.5 cc. (150,000 units) was administered once daily until all necrotic material, whether soft tissue or bone, had sloughed to leave a clean surrounding area. In some patients, this was continued for as long as two months. The effect on the child's general condition was, even in subsequently fatal cases, dramatically rapid, the toxaemia and temperature both subsiding. This effect of penicillin has also been reported by Schrand[3] and others; more recently, Ampofo and Findlay[4] have described similar results with oral aureomycin. Without antibiotic therapy, death results from toxaemia or intercurrent infection. The maximal degree of gangrene is attained early and appears to be self-limited. There is no tendency to local progression after this in both treated and untreated cases. Penicillin checks the actual spread of the infective necrotic process only if given in the pregangrenous stage; acting, in late cases, on the associated bronchopneumonia and by diminishing the bacterial toxaemia.

A high protein diet was given in all cases, mainly in the form of liver soup and dried or evaporated milk. All oral treatment had to be introduced gradually to avoid producing diarrhoea. As the children improved, meat, liver, fish and oranges were given. In view of probable vitamin B complex deficiencies, injections of crude liver extract were given twice weekly, together with yeast orally, either in a dried or liquid form. Antimalarial treatment, oral iron and cod liver oil were administered later, while "de-worming" was undertaken during convalesence. It must be emphasized, however, that the two main factors in treatment were penicillin and milk.

In many cases a long stay in hospital was necessary, sometimes up to three months. The usual cause of delay was the slowness of separation of the bony sequestrum. The mortality for the whole series was about 30%, although among patients in Stage II the death rate was almost 50%. The usual causes of death were toxaemia, bronchopneumonia, enteritis or varying combinations of these. In many instances, children were brought in for

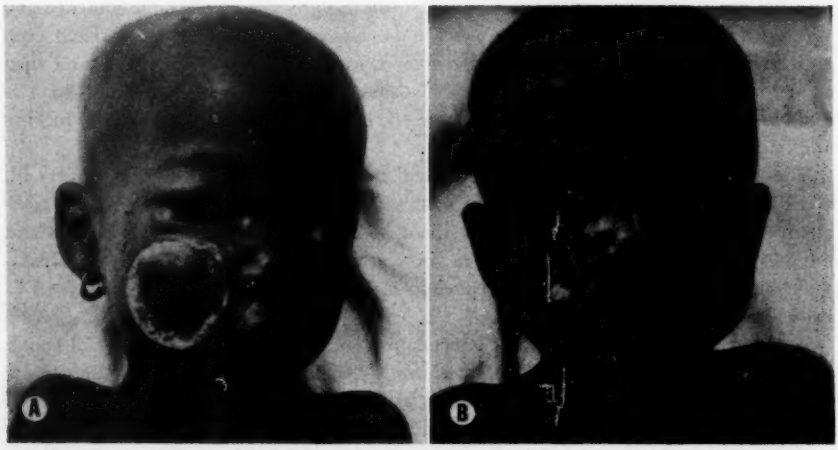

Fig. 1. A. On admission. Grossly malnourished Yoruba girl aged about 3½ yr. Gingivitis, infected necrosis of right maxilla with contact gangrene of right cheek. B. After 6 wk.' treatment. Soft tissue has sloughed, leaving huge cavity, which is now closing spontaneously. Four teeth and small sequestrum removed. Remarkable healing without plastic repair. Slight keloid formation.

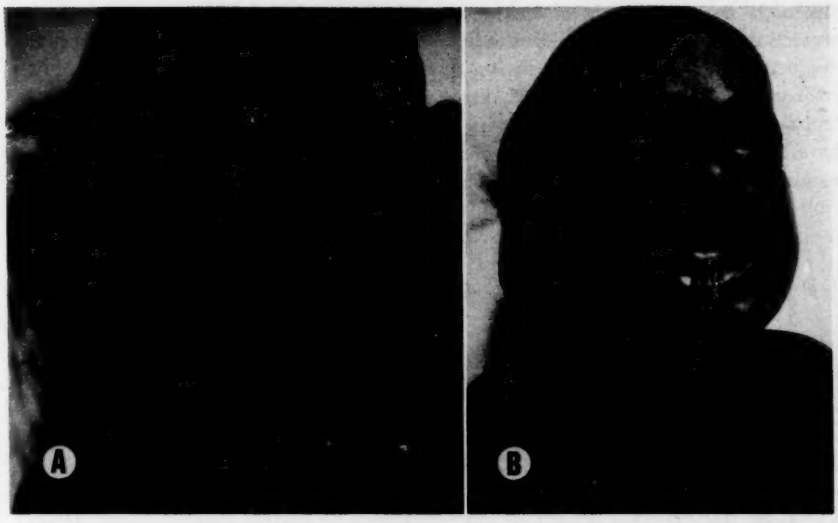

FIG. 2. A. On admission. Grossly malnourished Yoruba girl aged about 4 yr. Marked gingivitis and extensive necrosis of right mandible. Clearcut area of gangrene right chin. B. After 12 wk.' treatment. Great improvement in nutrition and general condition. Separation of gangrene with subsequent spontaneous closure of soft tissue gap. Almost whole of necrotic lower jaw removed, leaving only residual rim of mandible.

treatment late owing to apathy or mistrust on the mothers' part, or because of the long distance from the village to the hospital. Some had been treated for long periods by native witch doctors.

In many cases, once the necrotic debris was removed, the natural reparative power of the child's tissues was capable of producing a remarkable degree of spontaneous healing without any attempt at surgical assistance. Unfortunately in others, the extent of tissue loss was considerable and left a gaping cavity leading into the mouth, through which saliva and food dribbled. These cases presented great difficulty, as plastic repair, with necessarily prolonged hospitalization and ultra-sterile technics, is beyond the facilities of most tropical African hospitals. This type of case had to be discharged with a persistent deformity, covered with a bandage and pad to "hide" the deficiency as well as possible.

In some children the late appearance was not dissimilar to that of "granulomatous ulceration of the midline facial tissues" described by Williams,[5] although the clinical history and relatively frequent response to simple therapeutic procedures were quite different.

Two patients are shown in Figs. 1 and 2.

DISCUSSION

Cancrum oris is now a rarity in temperate countries, as is stressed by most pediatric textbooks, although occasional cases are seen in Europe and North America. In the tropics, however, the condition is still widespread. In the last 10 years, cases have been reported from the Philippines,[6] Turkey,[7] China,[8] Palestine,[9] South Africa,[8] India,[10]

Algeria,[11] Brazil,[12] Northern Rhodesia[13] and the Gold Coast.[4] In addition, in the writer's experience the condition has been found commonly in all the countries of the West African coast, in Egypt, the Sudan, Abyssinia and the Congo.

Cancrum oris in children in temperate countries is usually a complication of rubeola, typhoid, typhus, etc. In the tropics this does not appear to be the case. Occasional cases have been reported in patients with kala azar, particularly during treatment, and also in monkeys experimentally infected with leishmaniasis. This may be due to the low white

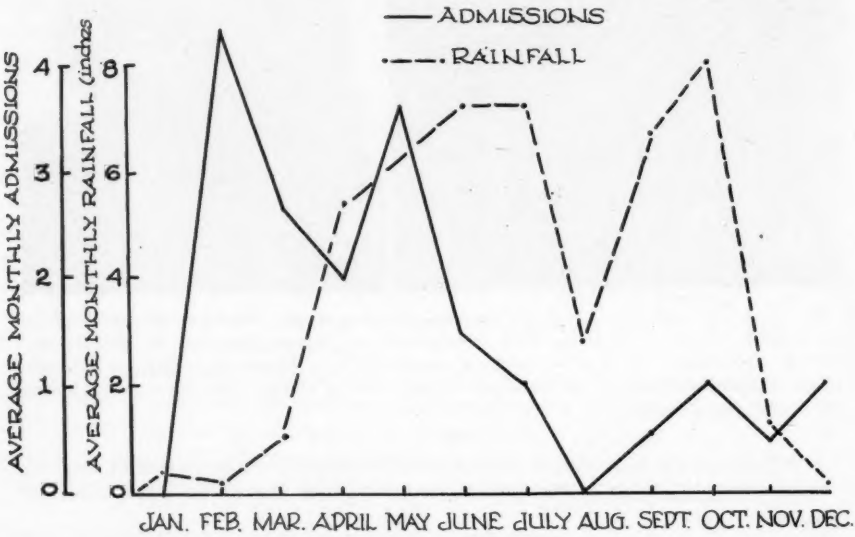

CHART 1. Graph showing relation of rainfall and admissions to hospital with infective gangrene of mouth—January 1949 to May 1951.

blood count seen in kala azar, particularly as rare cases of cancrum oris have been described with agranulocytosis due to sulphonamide and arsphenamine poisoning. Dias and Nobrega have recorded a case of cancrum oris in a child suffering from Chagas's disease.[12] However, in the majority of cases reported from the tropics, there seems to be no relation to any specific illness.

In almost all examples of infective gangrene of the mouth seen by the writer in Nigeria and elsewhere, malnutrition has been a constant feature. This has also been emphasized by most other observers. The age at which cases occur in Ibadan coincides with a period of active growth when the diet consists almost entirely of carbohydrate and water.

In Ibadan the year may be roughly divided into two periods, the rainy season from May to November and the dry season from December to April. As can be seen in chart 1, these patients are admitted more frequently at the end of the dry season and at the beginning of the rains. This is the end of the period of maximum food shortage and the time of year when any malnutrition is most likely to become clinically manifest.

The bacteriology of infective gangrene of the mouth does not seem to be clearcut. Facilities were not available for bacteriologic examination of all cases. In the 24 investi-

gated, 18 (75%) were found to show Vincent's organisms, together with a variable mixture of other bacteria. No evidence of oral leishmaniasis was found. As in other conditions associated with the presence of Vincent's organisms, it is difficult to be certain of their exact significance. However, many writers have reported this symbiosis in cases of cancrum oris, while Eckstein[7] found Vincent's organisms in fluid aspirated from presumably healthy tissue adjacent to the gangrenous area. According to many authorities, gingivitis, due to Vincent's organisms may be partially attributable in some cases to avitaminoses, probably of the vitamin B complex. Thus, Earle was of the opinion that the oral fusospirochoetosis commonly seen in parts of Peru was due to a lack of the vitamin B complex.[14] In addition, experimental evidence has shown that a deficiency of vitamin B_2 in monkeys tends to product an increase of the fusospirochoetal flora of the mouth with the development of Vincent's stomatitis.[15]

While the fundamental etiology of infective gangrene of the mouth remains in doubt, it is felt that the sequence of events may be as follows: After a prolonged period of general malnutrition, and in particular protein and vitamin B privation, the child develops a Vincent's gingivitis. In many instances, this infection may proceed no further. Cases of this type are seen commonly in the outpatients and respond rapidly to penicillin. In the malnourished, the infective process may spread along the roots of the teeth to involve the underlying maxilla or mandible, with subsequent bone necrosis (Stage I). Again the infection may halt, but in more severe cases, may spread from the area of bony inflammation to the adjacent soft tissues by direct contact. Gangrene of the inner surface of the cheek results, which advances peripherally and through the thickness of the soft tissue (Stage II). This is a rapid process, the full extent of the necrotic area being apparent almost at once.

Summary

The clinical features of infective gangrene of the mouth are described as seen in malnourished children in Ibadan, Nigeria. The etiology is discussed with reference to malnutrition in general and seasonal food shortage in particular. Successful treatment with a remarkable degree of natural healing occurred with penicillin and a high protein diet.

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SPANISH ABSTRACT

Gangrena Infecciosa de la Boca (Cancrum Oris)

En muchos países tropicales y especialmente en los niños pequeños, se han descrito diversos tipos de lesiones gangrenosas de la boca y de la cara, consideradas en conjunto bajo el término de "cancrum oris." En el presente trabajo se utiliza, por considerarla mas adecuada, la denominación de gangrena infecciosa de la boca.

El actual estudio se realizó con 53 niños Yoruba, de la población nativa de Ibadán, en la Nigeria Occidental, hospitalizados entre enero de 1949 y mayo de 1951. Su edades variaron entre 2 y 5 años, la edad promedio de iniciación fué alrededor de los 3 años. Todos habían tenido, por un período que varió entre 6 meses y 2 años, una dieta francamente deficiente en proteínas. Frecuentemente reportaban las madres, que por una o dos semanas, había habido aumento de la salivación, edema de la boca, fiebre y ulceración marginal gingival. Como síntomas tempranos en cerca del 50% de los pacientes existió diarrea y tos.

Los casos aquí reportados de gangrena infecciosa de la boca, clínicamente cáen dentro de dos grupos: aquellos que se encontraban en el estadio primero mostraron exclusivamente gingivitis y necrosis infeccioso del hueso, y los que se hallaban en el estadio segundo, con gingivitis, necrosis ósea y además grados diversos de gangrena de los tejidos blandos de la cavidad oral.

Como tratamiento se utilizó penicilina procaínica, a razón de 150.000 U. una vez al día, hasta que todo el material necrótico se había desprendido dejando una área limpia. El efecto sobre el estado general, aún en casos posteriormente fatales, fué rápidamente benéfico, mejorando la toxemia y la fiebre.

La máxima extensión de la gangrena aparece prontamente y no tiene tendencia a progresar, ya sea que se haya instituido tratamiento adecuado o nó. La penicilina detiene el avance del proceso infeccioso necrótico, solamente en el estado pre-gangrenoso.

Como parte del tratamiento hay que incluir así mismo a la inyección de extracto hepático 2 veces por semana, a la administración de levadura de cerveza por vía oral y a la dieta hiperproteíca. Debe enfatizarse que los dos principales factores en el tratamiento fueron la penicilina inyectada y la leche de la alimentación.

La mortalidad fué de 30% para la serie global, pero para aquellos enfermos en el estadio segundo del padecimiento fué de casi el 50%.

Algunos niños presentaron un grado notable de cicatrización espontánea de la zona gangrenada, mientras que en otros quedó un orificio que comunicaba el exterior con la cavidad bucal y presentaba un difícil problema para su reparación plástica.

Aunque permanece dudosa la etiología de la gangrena infecciosa de la boca, se piensa que la secuencia de los acontecimientos podría ser la siguiente: después de un estado prolongado de desnutrición, y en particular de privación proteíca y de vitamina B, el niño desarrolla una gingivitis de Vicent, que en muchos casos no progresa, pero que en el desnutrido se extiende a lo largo de las raíces del diente, afectando el maxilar y produciendo necrosis ósea subsecuente (estadio primero). La infección puede detenerse en este momento, pero en los casos mas serveros ataca por contacto directo a los tejidos subyacentes, resultando en gangrena de la superficie interior de la mejilla que avanza hacia la periferia y hacia el espesor de los tejidos blandos (segundo estadio).

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ACUTE BENIGN PERICARDITIS IN CHILDHOOD: COMPARISONS WITH RHEUMATIC PERICARDITIS, AND THERAPEUTIC EFFECTS OF ACTH AND CORTISONE

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SINCE the initial description by Barnes and Burchell[1] in 1942, numerous reports[2-21] have appeared in the medical literature dealing with a form of acute pericarditis which is unrelated to any other disease process classically associated with an inflammation of the pericardium. While many of these reported cases have occurred in young adults, the disease has not, as far as is known, been described in children heretofore. It is the authors' purpose, therefore, to present six instances of this syndrome occurring in patients within the pediatric age group and to discuss briefly some of the problems involved in the etiology, differential diagnosis and treatment of this condition. In the case of four of the patients, observations will be presented of the therapeutic effects of ACTH or cortisone, the use of which has not been previously reported in this disease. Finally, comparisons will be made between benign pericarditis and rheumatic pericarditis in children.

Many of the clinical and pathologic characteristics of this relatively new disease entity may be appreciated by merely reviewing the adjectives employed thus far in its nomenclature. The title pericarditis has been variously modified by such terms as benign, nonspecific, primary, idiopathic, cryptic, nonsuppurative and serofibrinous. As it occurs in adults, the disease is apparently a uniformly nonfatal, primary, sterile inflammation of the pericardium, characteristically marked by chest pain which is usually associated with fever. In the majority of cases, there is a pericardial friction rub as well as tachycardia and cardiac enlargement. Electrocardiographic alterations characteristic of pericarditis, such as S-T segment elevation and T-wave inversion, are found in almost every case. In about half the reported cases in adults there has been an associated pleural effusion, and in some instances roentgen evidence of pneumonitis. The erythrocyte sedimentation rate (ESR) is almost invariably elevated, and leukocytosis is present in a variable percentage of cases.

Benign pericarditis has been found to occur under a rather wide variety of circumstances. The disease has been noted to follow many respiratory tract infections, such as sinusitis,[22] pharyngitis,[14, 23] tonsillitis,[14] nasopharyngitis,[14] and atypical pneumonia.[24, 25] Bing[26] in 1933 reported an epidemic of acute pericarditis in Copenhagen consisting of six cases admitted to a single hospital ward within several weeks, each with a diagnosis of Barnholm's disease or epidemic myositis. Pericarditis of a benign nature has also been reported as a postoperative complication of various surgical procedures.[27, 28] A similar picture has been reported as part of an allergic carditis associated with serum sickness following the

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injection of tetanus antitoxin and other foreign proteins.[23, 29] A benign case of pericarditis and pleurisy with effusion occurring apparently spontaneously in a hypersensitive individual has also been described.[30]

Reasoning from the above associations, two mechanisms have been mentioned to explain the etiology of primary pericarditis: first, that the disease is of an infectious nature, probably nonbacterial and presumably viral in origin, and second, that the disease is the result of the reaction of the pericardium as a shock organ to an unknown offending allergen in a hypersensitive individual. Considerable evidence exists in favor of an infectious etiology.[7, 26] That viral agents may cause a benign pericarditis as part of a systemic infection has been demonstrated in the case of lymphogranuloma venereum,[31] but tests for antibodies to several other viral agents have yielded negative results[20, 24] in this disease.

The treatment of acute primary pericarditis in adults has been confined to symptomatic measures except for the recent trial of antibiotics. Of these, only aureomycin has given any indication of possible therapeutic value.[8, 32]

Clinical Observations

The 6 patients with acute benign pericarditis studied were all observed initially during a 1 yr. interval beginning in the spring of 1950. Each resided and was hospitalized in the Philadelphia metropolitan area, 2 at The Children's Hospital of Philadelphia, 2 at the Chestnut Hill Hospital and 2 at the Cooper Hospital in Camden, N.J. The age of the patients at the onset of their illnesses varied between 3 and 12 yr. Three were males and 3 females; all were white, although a Negro child with the disease has also been observed recently. The 8 patients with rheumatic pericarditis mentioned in the discussion for purposes of comparisons were observed concurrently in the same group of hospitals during approximately the same time interval. Because of considerations of space, only 2 typical case reports of benign pericarditis will be presented, with a summary of the findings in the entire group.

Case Reports

Case 1: C. S., an 11 yr. old white female, was admitted to The Children's Hospital of Philadelphia with a chief complaint of fever, chest pain and general malaise. There was no personal or family history of rheumatic fever.

The patient's illness began 12 days prior to admission, with abdominal pain, headache and malaise. These symptoms persisted for 3 days and were followed by a fever which ranged between 38.3° C. and 39.4° C. until the time of admission. There was intermittent pain in the back, left groin and in both feet, but no definite joint swelling, tenderness, heat or redness. She remained constantly fatigued. For 2 days prior to admission she complained of substernal pain and a slight productive cough. She was more comfortable in the sitting than in the supine position during this interval. The illness was considered to be "grippe" and was treated with 3 intramuscular injections of procaine penicillin plus administration of one of the sulfonamide drugs. She was slightly improved and had a normal temperature for 48 hr. prior to admission.

Physical examination on admission revealed a well developed, well nourished 11 yr. old white female who appeared acutely ill and uncomfortable. She was moderately dyspneic and orthopneic; the skin and mucous membranes had a greyish tinge. The heart was found to be markedly enlarged to the left. The heart sounds were distant and no murmurs were audible. The cardiac rate was 100/min., the blood pressure was 114/68 and the temperature was 38.7° C. Several hours after admission a pleuro-pericardial friction rub was heard over the sternum, and on the following morning a definite to-and-fro pericardial friction rub was clearly present. The liver was palpable 6 cm. below the right costal margin and was definitely tender. There was no peripheral edema nor any pulmonary rales.

Hospital Course: On admission the patient had early evidence of congestive heart failure and digitalization was begun. When this was approximately half completed the pericardial friction rub was discovered and the diagnosis of benign, nonspecific pericarditis considered. Digitalis was stopped and aureomycin begun. On this drug, in addition to aspirin, oxygen and other symptomatic measures,

the patient seemed to improve slightly. However, on the 4th hospital day there was a definite change for the worse, with a temperature rise to 39.4° C., return of dyspnea with respirations of 50/min., increase in heart rate to 132/min. and appearance of a gallop rhythm with muffled heart sounds. The patient was apprehensive and complained of precordial pain. At this point it was decided to try a course of ACTH therapy. After an initial dose of 30 mg., the patient was given 20 mg. every 6 hr. for 2 days and then the dosage was gradually reduced over a period of 3 more days, after which it was entirely discontinued. Response to this measure was dramatic, with fall of temperature, pulse and respiration to normal within 36 hr. The heart sounds became louder and the pericardial friction rub more difficult to hear until it finally disappeared 1 wk. after the beginning of ACTH therapy. Subjective symptoms also disappeared promptly with the use of hormone therapy. The patient remained asymptomatic until the time of discharge on the 18th hospital day. No cardiac murmurs were audible at any time during the hospitalization. Laboratory findings were not remarkable, except for an ESR (corrected for anemia) of 93 mm./hr. on admission, which fell to a value of 24 mm./hr. shortly before discharge.

Roentgen Findings: RGs of the thorax taken on the first and third hospital days showed extreme enlargement of the heart, obscuring the left lower lung field. In the lateral view the cardiac enlargement seemed to be in both the anterior and posterior directions. Films taken subsequent to ACTH therapy showed some decrease in heart size, which has remained at a top normal level to the present. The lung fields were consistently clear.

Electrocardiogram: Tracings taken on the first and second hospital days demonstrated slight elevation of the S-T intervals in leads 2 and 3. The T-waves were of low amplitude on the first day and inverted in all limb and precordial leads on the second day. These abnormalities persisted for at least 3 wk. but disappeared in subsequent examinations. Her tracing is now normal except for a top-normal P-R interval which has been present throughout.

Case 2: S. P., a 7 yr. old white male, was admitted to the Cooper Hospital, Camden, N.J., with a chief complaint of fever and pains in all extremities. There was no personal or family history of rheumatic fever.

Ten days before admission the patient was reported to have had an upper respiratory tract infection with a sore throat. During the week before entry, he experienced several minor and 2 major episodes of epistaxis. The pains in the extremities were vague and generalized, not associated with joint swelling or tenderness. During the 3 days prior to hospitalization, a temperature elevation to 38.3° C. appeared. Hospitalization was recommended with a provisional diagnosis of acute rheumatic fever.

Physical examination on admission revealed an acutely ill, extremely irritable and uncomfortable boy with a temperature of 40.0° C. There was discomfort on palpation or movement of all of the extremities, but no joint swelling, redness or heat was present. The lungs were clear except for the presence of a few scattered rales at the left base posteriorly and a pleural friction rub in a localized area over the left anterior chest wall. The heart rate was 140/min. and no cardiac murmurs were audible. The abdomen was soft and no organs or masses could be palpated.

Hospital Course: Initially the patient was treated with aspirin without relief of the extremity pain or subsidence of the fever. On the third hospital day a to-and-fro pericardial friction rub was heard at the base of the heart and the patient complained of precordial pain. Cardiac murmurs remained absent throughout. On the seventh hospital day the patient was started on a 3 wk. course of cortisone therapy at a dosage level of 150 mg./day for 2 days, followed by a maintenance dose of 100 mg./day, intramuscularly. Although the pericardial friction rub disappeared prior to the onset of therapy, the clinical response to this medication was dramatic in many respects. The temperature dropped to normal levels within 48 hr., the patient's appetite became ravenous and the pulse rate slowed to an average of 100/min. The child showed an abrupt change in personality which was conspicuous by contrast to his previous irritability and discomfort. Toward the end of the 3 wk. course of cortisone therapy rounding of the facial contour, marked interstitial fluid accumulation, acne, abdominal distention and moderate hepatomegaly appeared. Several injections of a mercurial diuretic were employed to control the weight gain due to fluid accumulation.

During the 3 wk. period following the cessation of cortisone administration, there was a gradual return of extremity pain, fever and tachycardia associated with anorexia and irritability. At this point, a 2 wk. course of ACTH therapy was begun at a dosage level of 100 mg./day, followed by a maintenance dose of 60 mg./day, intramuscularly. Once again the patient quickly became asymptomatic and

afebrile, with return of appetite and good spirits. Withdrawal of ACTH was not followed by a return of symptoms or signs of active disease.

Laboratory data were not remarkable except for a WBC count of 11.7 thousand/cmm., and an ESR (corrected) of 91 mm./hr. This value fell to 14 mm. 10 days after the onset of cortisone therapy, and rose again to 85 mm./hr. It fell again to 12.5 mm./hr. during the course of ACTH administration and remained at this level to the time of discharge.

Roentgen Findings: A chest film taken on admission showed normal lung fields and a heart which appeared questionably enlarged in the transverse diameter. A second film taken at the time of appearance of the pericardial friction rub 4 days later demonstrated cardiac enlargement and some haziness over both lower lung fields.

Electrocardiograms: A tracing taken on admission was reported to be within normal limits. A second tracing taken 3 days later was reported to be abnormal, with findings suggestive of pericarditis. T_1 and T_2 were inverted. ST_2 and ST_3 were elevated.

TABLE 1

CLINICAL SUMMARY OF 6 CHILDREN WITH ACUTE BENIGN PERICARDITIS

	C. S.	S. P.	E. F.	P. P.	N. L.	D. D.
1. Antecedent resp. tract infection	0	+	+	+	0	0
2. Precordial pain	+	0	0	+	0	0
3. Pericardial friction rub	+	+	+	+	+	+
4. Pain in extremities	+	+	+	+	0	+
5. ECG findings characteristic of pericarditis	+	+	+	0	+	0
6. Cardiac enlargement	+	+	0	+	0	+
7. Pleural or pulmonary involvement	+	+	0	+	0	+
8. Congestive heart failure	+	0	0	+	0	+

+ = presence of clinical feature
0 = absence of clinical feature

Clinical Features of Acute Benign Pericarditis in Childhood: The illness of 3 of the 6 patients was preceded by a respiratory tract infection. Two of the 6 patients complained of precordial pain, these being the oldest in the group, from whom better reporting of symptoms might be anticipated. A pericardial friction rub was audible in all 6 instances, usually at the peak of the clinical course. The friction rub was often not detected until several days following the onset of symptoms. A temperature elevation varying between 38.4 and 40.0° C. was commonly present at the same time as the pericardial friction rub. A tachycardia ranging between 120 and 140 beats/min. also accompanied the acute febrile state. At this point the children were usually irritable, anorexic, toxic and suffering general malaise. The classical electrocardiographic changes associated with pericarditis[33, 34] were present in 4 of the pediatric cases. In one of the others it was obscured by the presence of a Wolff-Parkinson-White electrocardiographic configuration. Cardiac enlargement as demonstrated by roentgenographic studies was observed in 4 of the 6 patients. Pleural or pulmonary involvement was associated with pericarditis in 4 instances. Pain in the extremities was observed in 5 of the 6 patients. In most instances it was of a diffuse, generalized nature and suggested the presence of a widespread myositis as part of the total disease process. In no instance was the pain confined to the joints, nor was there ever any joint swelling, redness, heat or tenderness. Three of the patients also showed clinical evidence of early congestive heart failure. The disease was not seen in children below the age of 3 yr., and most of the cases occurred during the latter half of childhood. A summary of the clinical findings is presented in table 1. Marked elevation of the erythrocyte sedimentation rate was found in 5 of the 6 children on admission to the hospital, whereas 1 child was reported to have a normal ESR during the acute phase of her illness. The initial WBC count at the time of admission varied between 5.0 and 34.0 thousand/cmm. The differential counts were not remarkable and showed only a mild shift to the left.

Therapeutic Effects of ACTH and Cortisone: Initially, all the patients received the conventional symptomatic type of therapy plus one or more of the antibiotic drugs. Five of the 6 patients received either aureomycin or chloramphenicol in full doses. In 4 instances the lack of clinical response and the critical condition of the patient seemed to warrant a trial of either ACTH or cortisone. Initially, two of these children received approximately 10 day courses of ACTH, while the other 2 received 1 wk. and 3 wk. courses of cortisone, respectively, both hormones being administered intramuscularly at the dosage level conventionally employed in the treatment of rheumatic fever. In all instances the eventual outcome was a favorable one, but in each of the hormone-treated cases there was clear evidence of an alteration in the disease process during the period of administration of the drug. In each child receiving either ACTH or cortisone a dramatic clinical improvement occurred within 48 hr. of the onset of therapy. In one ACTH-treated case (Case 1), this benefit was apparently maintained after withdrawal of the drug, while in the other 3 instances a definite reappearance of symptoms occurred after cessation of drug administration. The other ACTH-treated patient remained well after a second course of the hormone. One of the cortisone-treated patients (Case 2) received a 10 day course of ACTH when his disease reappeared following withdrawal of cortisone. No relapse followed withdrawal of the ACTH.

Administration of either drug on each occasion was accompanied by a prompt return to normal levels of the previously elevated temperature curve and the disappearance of limb pain, malaise and symptoms of general toxicity. These were replaced by a feeling of well-being which sometimes bordered on euphoria. Anorexia was replaced by an excellent appetite. The erythrocyte sedimentation rate dropped from markedly elevated to normal levels within 7 to 10 days.

The evidences of cardiac improvement in the 4 hormone-treated patients were less striking. A slowing of the cardiac rate occurred, which may have been associated in part with return to normal of the temperature level. In the 2 cases in which a pericardial friction rub was present at the start of hormone therapy, these persisted for 7 and 12 days, respectively. In 2 other cases it disappeared before therapy was started and in no instance did it reappear upon withdrawal of hormone therapy when a flare-up of other signs and symptoms occurred. In the 2 untreated cases the pericardial friction rub was audible for 2 and 7 days, respectively. The cardiac enlargement which was present in each of the treated cases disappeared, but not until several weeks after the conclusion of hormone therapy. No cardiac enlargement was present in the untreated patients. The ECGs in both the treated and untreated cases resumed their normal configuration approximately 1 mo. after the onset of the disease. Congestive heart failure was present in 3 of the children treated and improved rapidly during the course of hormone therapy.

The duration of illness in the 6 children varied from 3 wk. to 3 mo., which is in close agreement with that of adults. The longest occurred in the youngest patient, who received a single 8 day course of cortisone therapy. The illness of shortest duration was experienced by one of the children not treated with either of the hormones.

Late Clinical Observations: Up to the present there has been an opportunity to follow the 6 children mentioned above for periods ranging from 10 to 22 months from the onset of their respective illnesses. Our initial recommendations for convalescent care were conservative and simulated the scheme widely employed in the care of convalescing rheumatic cardiac patients. (The necessity for such conservative management in this disease is perhaps open to question.) Physical examination at present reveals no evidence of heart disease in any of these children except for the appearance in a single case of a peculiar, faint, squeaking adventitious sound, which has been heard only during the course of intercurrent febrile illnesses. Roentgenographic studies reveal cardiac enlargement in none of these children while all have normal electrocardiographic tracings (except for one child who demonstrates a Wolff-Parkinson-White configuration, probably the result of a congenital abnormality). In another child rather frequent extrasystoles are now present which had their onset during the acute phase of her benign pericarditis.

Discussion

Acute Benign Pericarditis and Acute Rheumatic Pericarditis: In the literature dealing with acute benign pericarditis in adults the differentiation of this condition from acute coronary occlusion with myocardial infarction has been emphasized.[1, 3–5, 19, 21] In the pediatric age group, coronary occlusion is almost nonexistent and the differentiation from

rheumatic pericarditis, with its markedly different prognosis, is the salient problem.

A question might indeed be raised as to whether cases such as those reported here might represent an isolated pericarditis of rheumatic etiology without accompanying myocarditis or endocarditis, although the occurrence of such a lesion has never been demonstrated at necropsy. In our present state of knowledge the final answer to this question would necessarily depend upon studies of pathologic material, but the benign nature of the disease reported has precluded such investigation. It is, however, possible to demonstrate a distinct clinical difference between acute rheumatic pericarditis and acute benign pericarditis by means of a simple comparison of the six cases of the latter with eight definite episodes of rheumatic pericarditis observed concurrently by the authors during the same time interval in the same geographic area. Although the number of cases involved in this comparison is too small to provide statistically significant differences, these differences are striking and almost certainly meaningful. Of the eight cases of rheumatic pericarditis mentioned, each was associated with the appearance of at least one or more cardiac murmurs of the organic type. All eight of these rheumatic children were found to have apical systolic blowing murmurs, four demonstrated aortic parasternal diastolic murmurs and five were found to have apical diastolic blowing murmurs at some time during the acute phase of their illness. These adventitious sounds were assumed to indicate endocardial involvement by the rheumatic process or possibly dilatation of the fibrous ring surrounding the valve orifices involved. In contrast, no murmurs of the organic type were audible in any of the children with benign pericarditis. Again, in each of the eight patients with rheumatic pericarditis at least one or more of the major or minor criteria of Jones[35] for the diagnosis of rheumatic fever were present, in addition to carditis. Six of the rheumatic patients experienced a migrating polyarthritis, one had epistaxis and three had experienced previous attacks of rheumatic fever. In the group with benign pericarditis, on the other hand, none had a past history of rheumatic fever, although one child gave a positive family history of the disease. Five of these children complained of pain in the extremities, but at no time was there any definite evidence of acute arthritis as manifest by joint swelling, tenderness, heat or redness. In two instances of apparent shoulder pain, the presence of a pleural effusion with resulting referred pain to the ipsilateral shoulder region provided an adequate explanation. In the other three cases a myositis associated with such a febrile illness could readily account for the symptoms. The administration of aspirin to these latter patients did not significantly relieve their myalgia, as would be expected in instances of rheumatic arthritis. None of the major symptoms of rheumatic fever were present in the patients with benign pericarditis, and only a single instance of a minor symptom, epistaxis, occurred. Also, among this group there were no deaths, while three of the eight (38%) patients with rheumatic pericarditis succumbed during the acute episode. Of the five patients who survived, four now have persisting apical systolic murmurs, one an aortic diastolic murmur and four show evidence of cardiac enlargement, after a follow-up period that averages one year. In the benign group none of the children have residual murmurs nor evidence of cardiac enlargement. Thus, differences in the incidence of endocarditis, in the presence of associated signs and symptoms of rheumatic fever, in mortality rate, and in the evidences of cardiac residua all suggest that distinctly different disease processes were present in these two groups of patients. This contrast is summarized in table 2.

Finally, the serologic evidence does not favor a diagnosis of rheumatic pericarditis in the patients presented here. Sera of these six children were tested for their titer of two of

TABLE 2

	Primary Pericarditis		Rheumatic Pericarditis	
	No. of Patients Total: 6	% of Total	No. of Patients Total: 8	% of Total
1. Incidence of murmurs during acute episode	0	0	8	100%
2. Incidence of cardiac enlargement during acute episode	4	66%	8	100%
3. Incidence of residual murmurs	0	0	4	80%*
4. Incidence of residual cardiac enlargement	0	0	4	80%*
5. Deaths	0	0	3	37%
6. Previous attacks of rheumatic fever in history	0	0	3	37%
7. Incidence of associated major or minor criteria for diagnosis of rheumatic fever	1†	17%	8	100%

* Three of the 8 patients with rheumatic pericarditis died leaving only 5 for evaluation of residua.
† Epistaxis.

the antistreptococcal antibodies, antihyaluronidase and antistreptolysin O. The titers observed varied within the range for normal individuals or those having recent streptococcal infections. None of the titers were sufficiently high to fall within the range which is reasonably suggestive of rheumatic fever. This finding is of additional significance in view of the fact that among the antihyaluronidase titers determined in sera of patients with rheumatic carditis at the Rheumatic Fever Laboratory of The Children's Hospital of Philadelphia, those of patients with active pericarditis have been among the highest found.

Possible Etiologic Relationships of Acute Benign Pericarditis: As was mentioned above, several of the authors who described this disease in adults have suggested a possible viral etiology, in particular a relationship with some virus of respiratory tract infections. Through the courtesy of the Virus Diagnostic Laboratory of The Children's Hospital of Philadelphia some studies in this direction were carried out. Sera were obtained at the outset of the disease and at intervals thereafter in the case of four of the six patients, and after the disease was established, in the case of a fifth patient. These were examined for the titer of cold agglutinins and for antibodies to the viruses of influenza A and B, lymphogranuloma venereum, psittacosis, Q fever, and two strains of group A and one strain of group B Coxsackie virus. None of the sera tested showed any high or rising titers which would indicate the presence of recent infection with any of these specific viral agents. This exploration has, of course, been limited to viruses among those for which a serologic test is available. It is quite possible that a specific viral agent of this disease may exist which is independent of those viruses which we know by virtue of their etiologic role in other diseases.

It is also not inconceivable that multiple etiologic mechanisms may be operating to produce the clinical picture of acute primary pericarditis, and that we are therefore dealing not with a specific disease but rather a clinical syndrome resulting from a variety of causative insults to the organs involved. Similarly, it is conceivable that we may be dealing here with a disease of hypersensitivity, and that a number of different offending allergens may be able to incite the reaction which results in an inflammation of the pericardium and the clinical picture of acute benign pericarditis. Certainly if the disease is caused by a

specific infectious agent, it is likely that this infection is a systemic one, although the disease has been named for its most striking manifestation, the inflammation in the pericardial sac. Pleural effusion has been observed, as recorded above, and the widespread pain in the extremities is quite suggestive of inflammation of skeletal muscle. It may then be that the fundamental inflammation is that of a mesenchymal tissue occurring anywhere within the body. Of such possible associations of acute benign pericarditis with a generalized infectious disease, that with an infectious myositis would seem to be most consistent with the clinical pattern which was observed in these patients. The apparent beneficial effect of ACTH and cortisone in this disease does not contribute toward clarification of its mechanism of etiology. Suppression of both inflammatory reactions and phenomena of hypersensitivity occur with the use of these hormones and thus either an infectious or allergic origin of the disease is compatible with the results of therapy.

Therapeutic Effects of ACTH and Cortisone in Acute Benign Pericarditis: The authors' experience in the treatment of these six patients has provided certain impressions. First, that the antibiotic drugs, including aureomycin and chloramphenicol, have no specific effect upon the course of acute benign pericarditis in children. Treatment with either ACTH or cortisone, on the other hand, produced a prompt and dramatic improvement in the clinical picture, with suppression of many signs of active disease during the period of administration of either of the two hormones. There was, however, no indication in this small group of patients that the natural course of the disease was permanently curtailed or its duration diminished by the action of the drugs. Thus, it appears that these agents may play a useful but limited role in the treatment of patients with acute benign pericarditis, especially in those cases which are of sufficient severity to lead to congestive heart failure. The suppression of the inflammatory process may aid in tiding these patients over the critical periods in the natural course of their disease.

In the case of rheumatic fever a similar concept of presumably nonspecific temporary suppression of the evidence of inflammation by ACTH and cortisone has been offered by the Mayo Clinic group.[36, 37] Although such a mechanism of protection of the susceptible organs from their unknown irritants, as postulated by Hench et al.,[37] may be operative in both these situations, the differences in the natural histories of the two diseases tend to create an apparent difference in the results of hormone therapy. Thus, in a self-limited illness of relatively short duration, such as acute benign pericarditis, a suppression of the inflammatory process may tide the patient over until the natural termination of the disease, giving an impression of cure by these hormones, whereas in the case of rheumatic infection, with its chronic, recurrent or fatal character and its frequent association with cardiac residua, the limitations of the therapeutic effect of these agents may be more apparent. This point is made because it may well have certain implications in the evaluation of the therapeutic effects of ACTH and cortisone in rheumatic carditis, since failure to recognize cases of acute benign pericarditis in a hormone-treated series of patients with rheumatic heart disease would give rise to a misleading impression of a therapeutic value of these agents in the latter disease.

Summary

Six cases of acute benign pericarditis in childhood have been studied.

The importance in childhood of the differentiation of acute benign pericarditis from acute rheumatic pericarditis has been emphasized and demonstrated by a comparison of the clinical findings and subsequent courses in patients with these two types of pericardial involvement.

The results of treatment of acute primary pericarditis with the hormones ACTH and cortisone are presented and discussed.

Some negative findings in the study of the etiology of this disease are presented.

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Additional Case Reports

Case 3: E. F., a 4½ yr. old white female, was admitted to the Chestnut Hill Hospital with chief complaints of fever, mild abdominal pain, headache and general malaise. There was no personal or family history of rheumatic fever. Her father had been confined at home with "grippe" for several days during the week prior to her illness. He had generalized aching pains but recovered uneventfully. The patient's illness was antedated by 3 moderately severe upper respiratory infections occurring 8, 5 and 2 wk. before the present illness. From each of these she recovered in 5 to 7 days and returned to play and school. Two days before admission she became febrile, complained of aching in her legs, but not in the joints, headache and vague abdominal pain.

Physical examination at that time revealed hypertrophic tonsils and a moderate pharyngitis. The lungs were clear. The pulse rate was 130/min. at the apex with frequent extrasystoles. These occurred at least once in every 4 to 7 beats. There was also a creaking friction rub heard just lateral to the apex. No murmurs were audible. The heart did not seem enlarged and the patient was in no distress.

Hospital Course: The temperature on admission was 37.8° C. Except for a single spike on the 7th hospital day, it never exceeded 37.8° C. The pulse ranged between 100 and 120/min. The child offered no complaints except for the abdominal pain already mentioned. She was given chloromycetin 150 mg. every 4 hr. After the second hospital day the friction rub was no longer heard. The arrhythmia, however, persisted and was present unchanged when she was discharged 10 days after admission. It was felt that the cardiac arrhythmia had developed in association with her illness and had not been present prior to that event.

Laboratory Data: Urinalysis was within normal limits. The blood count revealed Hgb. 13.7 gm./100 cc. and RBC count of 4.7 million/cmm. WBC count was 9.0 thousand/cmm. with 64% neutrophiles, 28% lymphocytes, 3% monocytes, 1% eosinophiles and 4% basophiles. Subsequent blood counts were all normal. ESR was 26 mm./hr.

Roentgen Findings: Chest RG revealed some impairment of translucency of both lung fields. The appearance was considered to be the result of engorgement of the pulmonary blood vessels rather than parenchymal disease. Although the cardiac shadow appeared slightly broader than usual at fluoroscopy, there were good cardiac pulsations.

Electrocardiogram: The tracing taken on admission was reported as follows: Rate: 125; Rhythm: many extrasystoles arising from various foci; P-waves: normal; P-R interval: 0.13 sec.; QRS.: normal; S-T interval: slight positive displacement in various leads; T-waves: inverted in various leads. Interpretations: Extensive pericarditis, probably active.

Subsequent Course: The patient was sent home and kept at bedrest for 2 wk., at the end of which time the ESR was found to be 9 mm./hr. The patient had been entirely afebrile, and the premature systoles were much less frequent. ECG taken a month after onset still showed the abnormal T-waves but was otherwise normal. Three months after onset the child showed only an occasional premature systole and had been returned to full activity. The length of her follow-up has now been 13 mo. and no evidence of cardiac disease can be found except for occasional extrasystoles.

Case 4: P. P., a 12 yr. old white male, was admitted to The Children's Hospital of Philadelphia for the first time with a chief complaint of fever and respiratory distress.

There was no family history of rheumatic fever. There had been no antecedent symptoms referable to the respiratory or cardiovascular systems except for several respiratory tract infections during the preceding winter, the last of these occurring 3 wk. before the onset of the present illness.

The patient's illness began 16 days prior to admission to The Children's Hospital of Philadelphia,

at which time he suddenly developed chills and fever. On the next day he complained of diffuse, intermittent pain and tenderness in all extremities. He failed to improve on a regimen of bedrest, aspirin, penicillin and sulfonamides administered at home and was therefore admitted to a local hospital. At this time he was dyspneic and orthopneic, and complained of precordial and epigastric pain. On admission flaring of the alae nasi and a greyish pallor of the skin were noted. The heart was found to be diffusely enlarged, and a loud to-and-fro friction rub was heard at the base. The heart sounds were difficult to hear. The liver was palpable 4 cm. below the right costal margin and was tender. Both lower extremities were tender to the touch. A chest film revealed diffuse enlargement of the heart. The patient was treated with oxygen, aspirin, para-amino benzoic acid, digitalis and sedatives. The pericardial friction rub disappeared and reappeared on several occasions during the next few days, as did a gallop rhythm. No definite cardiac murmurs were heard. The fever, limb pains and manifestations of cardiac failure persisted, and after a week in the local hospital it was decided to transfer the patient to The Children's Hospital of Philadelphia for ACTH therapy.

Physical examination on admission revealed a pale, well nourished, cooperative 12 yr. old white boy who was acutely ill. The temperature was 38.3° C. He demonstrated definite dyspnea and orthopnea. The respiratory rate was 50 to 60/min. and the pulse rate 100/min. The blood pressure was 105/50. The heart was markedly enlarged to the left and the heart sounds were distant. A friction rub was not present at this time. A soft systolic murmur could be heard in the second left interspace but no apical systolic or diastolic murmurs were audible. The liver edge was barely palpable. There was no evidence of joint swelling, tenderness, heat or redness.

Hospital Course: On the day of admission, ACTH in a dosage of 80 mg./day was started. The usual cardiac supportive measures such as oxygen, complete bedrest, low salt diet and limited fluids were also instituted. On the day following admission the temperature and pulse dropped to normal limits. The boy felt better subjectively and his appetite improved. This improvement was maintained throughout the course of ACTH therapy except during a brief episode of paroxysmal ventricular tachycardia which lasted several hours and was halted by the administration of oral quinidine sulfate 0.12 gm. The tachycardia was thought to be related to the patient's congenital abnormality in cardiac conduction mechanism which conformed to the electrocardiographic picture of the Wolff-Parkinson-White syndrome. Serial RGs of the chest revealed a progressive decrease in cardiac size and resorption of fluid from the left pleural fluid. The dosage of ACTH was cut to 60 mg./day on the 3rd hospital day and 40 mg./day on the 5th hospital day. From this level it was tapered off and stopped completely on the 9th hospital day. The ESR had descended from 67 to 27 mm./hr. in this interval. On the day following discontinuation of the ACTH the patient's temperature rose to 38.3° C. and continued to show daily spikes up to 38.3° to 38.8° C. during the next 4 days. Despite these temperature elevations and a rise of the ESR to 60 mm./hr., no further medication was given. The temperature and other signs mentioned gradually returned to normal and the patient was discharged on the 20th hospital day. At this time cardiac auscultation showed no abnormalities and the patient was asymptomatic.

Laboratory Data: Urinalysis was normal. The blood count revealed Hgb. 13.1 gm./100 cc., RBC count 4.45 million/cmm. WBC count 17.4 thousand/cmm. with a differential of 83% neutrophiles, 15% lymphocytes and 2% monocytes. Subsequent counts revealed only a lowering of the total WBC count. The ESR (corrected) was 67 mm./hr. on admission; 26 mm./hr. on 4th day; 8 mm./hr. on 8th day; 60 mm./hr. on 33rd day; and 27 mm./hr. on 37th day.

Roentgen Findings: On admission a chest film revealed marked cardiac enlargement and a fluid accumulation at the left base posteriorly. Six days later marked decrease in heart size was noted, but it was still considered to be enlarged beyond normal limits. The fluid in the left pleural space had resolved completely at this time. A film taken 3 wk. after admission showed no change in heart size.

Electrocardiogram: Except for the tracing taken during the episode of paroxysmal tachycardia all the tracings were similar, showing a shortened P-R interval and a prolonged QRS complex, findings typical of the Wolff-Parkinson-White syndrome. During the acute phase of the patient's illness there was also present a moderate left axis deviation which has subsequently reverted to normal. Because of this grossly abnormal ECG, it was impossible to detect the characteristic alterations associated with pericarditis.

Subsequent Course: The patient did well until approximately 2½ wk. after discharge. He then rather suddenly became lethargic, refused food and complained of pain in the left deltoid region.

On the following day he became dyspneic and complained of precordial pain. He was quickly returned to The Children's Hospital of Philadelphia and on admission a temperature of 38.8° C. was found. The cardiac rate was 150/min. and a definite gallop rhythm was audible at the apex. No cardiac murmurs were audible. The respiratory rate was 28/min. and deep in amplitude. A chest film showed moderate cardiac enlargement and fluid in the left pleural space. The liver was not palpable and there was no peripheral edema. The patient was again started on ACTH at a dosage level of 80 mg./day and again showed a dramatic response. The temperature dropped to normal on the 2nd hospital day and remained at this level until discharge 13 days later. The ACTH was given for 10 days in gradually diminishing doses. There was no recurrence of signs or symptoms on stopping the drug following this second course. No other medication was given except for a weak commercial broth to supplement the potassium intake during ACTH administration. Subsequent to the 2nd hospital admission, the patient has been well for a period of over 19 mo.

Case 5: N. L., a 9 yr. old white female, was admitted to the Chestnut Hill Hospital with complaints of fever, headache, vomiting and general malaise. There was no personal or family history of rheumatic fever.

Her illness began the day before admission with sudden onset of fever, headache, repeated vomiting and moderate coughing. A physical examination revealed no abnormal findings except those related to the heart. Her temperature was 38.3° C.; pulse rate was 80/min and regular. A rather loud squeaking friction rub was audible over the entire precordium. It could be heard faintly below the left scapula posteriorly. The heart was not enlarged and no murmurs were heard. Although the child was febrile and complained of headache and vague abdominal discomfort, she did not appear seriously ill at any time.

Hospital Course: She was referred to the hospital where treatment with aureomycin was begun at a dose of 150 mg. every 4 hr. The temperature on admission was 38.6° C. and never exceeded this level again. On the 5th day it went down to 37.0° C. and from then on it ranged from 37.0° to 37.8° C. Three days after admission the friction rub could be heard only faintly. After a week it was only audible intermittently. There was no clinical evidence of effusion. She was discharged to bedrest at home 16 days after admission.

Laboratory Data: Blood count on admission revealed Hgb. 13.5 gm./100 cc. with RBC count of 4.2 million/cmm. The WBC count was 5.0 thousand/cmm. with 62% neutrophiles, 36% lymphocytes, 1% monocytes and 1% eosinophiles. Urinalysis was within normal limits. A tuberculin skin test was negative. Repeated blood counts and urine examinations were normal. The ESR was 2 mm./hr. on 13th hospital day and was the same 1 mo. later.

Roentgen Findings: Chest film and fluoroscopic examination on the day of admission revealed no abnormalities of cardiac size or contour. The lung fields were also normal.

Electrocardiogram: The first ECG taken on the day after admission to the hospital was reported as follows: Rate: 92; Rhythm: regular; P-waves: normal; P-R interval: 0.15 sec.: QRS: normal; S-T interval: slight positive displacement in leads 1, 2, CR_3 and CR_4; T-waves: inverted in leads 2 and 3, low in CR 4, 5, 6. Interpretation: The changes are compatible with the diagnosis of pericarditis involving the posterolateral surface of the left ventricle. A tracing made 13 days later was within normal limits.

Subsequent Course: During 15 mo. of follow-up, the child has remained clinically well and has gained 4.1 kg. Physical findings have varied. With fever accompanying common colds, her friction rub has been audible. It may also be heard after exercise particularly when the child leans far forward. It is sometimes present at 1 examination and absent 1 hr. later.

Case 6: D. D., a 3 yr. old white male, was admitted to the Cooper Hospital, Camden, N.J., with a chief complaint of fever of 2 days' duration, irritability and nuchal rigidity.

Both parents were alive and well. There were 7 siblings, all of whom were living and well except a sister, who was reported to have had rheumatic fever. The patient had experienced only the common childhood contagious diseases and was considered to be in good health until the onset of the present illness.

Two days prior to admission he developed a fever which ranged up to 40.0° C. He was treated with sulfadiazine without clinical response. At this time meningitis was suspected because of extreme irritability and generalized muscle pain and spasm involving the neck, back and hamstring muscle groups. The child complained of pain wherever he was touched.

Physical examination on admission revealed an extremely irritable child with a temperature of

37.8° C. There was some redness and injection of the pharynx and tonsils. The anterior and posterior cervical lymph nodes were enlarged and tender. The neck was tender to touch but not truly rigid. The lungs were clear. The pulse rate was 120/min. and the respirations 28/min. No cardiac murmurs were audible. Neurologic examination was negative except for spasm and tenderness of the neck, back and hamstring muscles. There was no muscle weakness.

Hospital Course: A lumbar puncture was performed shortly after admission and revealed no cerebrospinal fluid abnormalities. The temperature returned to normal with no treatment but the muscle pain and spasm persisted. On the 4th hospital day some hepatic enlargement was noted. The liver size increased progressively for several days and was associated with ascites and dyspnea. On the 10th hospital day, roentgen examination of the chest revealed a markedly enlarged cardiac shadow suggesting a pericardial effusion and a small amount of pleural fluid in the left costophrenic angle. At this time the temperature again became elevated, spiking daily to 38.3° to 40.0° C. despite treatment with aspirin, penicillin and aureomycin. The area of cardiac dullness was enlarged to percussion and the heart sounds were muffled. By the 14th hospital day the clinical picture had not changed except for the appearance of a pericardial friction rub in the second right interspace. The venous pressure was elevated as measured directly at the anticubital vein and by the presence of distended cervical veins. Some spontaneous improvement occurred during the week that followed return of the temperature to normal. On the 20th hospital day an 8 day course of cortisone was begun at a dosage level of 50 mg./day intramuscularly. Gradual improvement continued and on the 24th hospital day diminution of the size of the cardiac silhouette was observed. The child became cheerful and active at this time. Ascites disappeared shortly thereafter but the liver was palpable until the 44th hospital day. The patient's general condition improved progressively and he was discharged in an afebrile and asymptomatic condition approximately 2 mo. after admission with no abnormal physical signs.

Laboratory Findings: Hgb. level varied between 55 and 71% while the RBC count ranged between 3.8 and 2.8 million/cmm. during the hospital course. WBC count on admission was 25.9 thousand/cmm. and rose to 34.4 thousand/cmm. before tapering off to normal values with recovery. The initial differential count revealed 84% polymorphonuclear leukocytes. The ESR was high prior to cortisone therapy, was significantly lower during the interval of cortisone administration, and returned to normal levels during convalescence.

Roentgen Findings: Fluoroscopic and radiographic examination of the chest on the 8th hospital day revealed marked enlargement of the silhouette. There was widening of the supracardiac shadow with the patient in the Trendelenburg position. The presence of a small amount of pleural fluid was suspected at this examination and confirmed on re-examination the following day. Four days later the cardiac shadow appeared unchanged and the cardiac pulsations were noted to be diminished in amplitude. A film taken 3 wk. after admission showed considerable diminution in the size of the cardiac shadow but persisting evidence of pleural fluid bilaterally. At this time there was some mottled increase in haziness over both lower lung fields. Seven weeks after admission the cardiac shadow was even smaller and resolution of the pleural fluid and lung densities was almost complete.

Electrocardiograms: A tracing taken on the 13th hospital day revealed a cardiac rate of 125/min., low amplitude T-waves which were inverted in the first limb lead, and a tendency toward left axis deviation. No deviations of the ST segment were noted. Subsequent tracings showed a gradual increase in amplitude of the T-waves, return of T_1 to the erect position and disappearance of the axis deviation.

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SPANISH ABSTRACT

Pericarditis Aguda Benigna en la Infancia; Comparación con la Pericarditis Reumática y Resultados Terapeúticos de la Hormona Adrenocorticotrópica (ACTH) y Cortisona

La descripción inicial de la pericarditis aguda benigna del adulto por Barnes y Burchel en el año de 1942 fué seguida de numerosas publicaciones en la literatura médica pero ninguna referente a niños. El objeto de este artículo es reportar 6 casos de este síndrome en la infancia y discutir su etiología, diagnóstico diferencial y terapeútica.

El cuadro en el adulto es de un padecimiento con inflamación primitiva del pericardio, esteril, que produce dolor precordial, frote pericárdico, taquicardia y cardiomegalia. El electrocardiograma muestra frecuentemente elevación del segmento S-T e inversión de T. Generalmente hay fiebre, y derrame pleural con o sin neumonitis, sedimentación eritrocítica elevada y leucocitosis. Aparece a continuación de infecciones respiratorias, en forma epidémica o bien después de un fenómeno alérgico a sueros medicamentosos, proteínas extrañas o hipersensibilidad individual. Consecuentemente se piensa que es de naturaleza infecciosa, quizas de origen viral o que obedece a un proceso alérgico, siendo el pericardio el órgano de choque.

Este grupo de niños presentó frote pericárdico, a veces varios días después del principio del cuadro, cinco se quejaron de dolor en las extremidades, que era difuso, muscular y nunca localizado a las articulaciones las cuales eran normales. Unos tuvieron dolor precordial, cardiomegalia con insuficiencia miocárdica, alteraciones electrocardiográficas características de pericarditis y participación pleural o pulmonar. En 3 enfermos hubo infección respiratoria previa. La sedimentación sanguínea muy elevada en el 80% de los casos y leucocitosis entre 5.000 y 34.400.

El "A.C.T.H." o la Cortisona produjeron descenso rápido de fiebre, desaparición de dolores, malestar y toxicidad, sensación de bienestar, a veces euforia, y apetito excelente. La sedimentación eritrocítica se hacia normal entre 7 y 10 días. Sin embargo, la mejoría del corazón fué menos notable y la cardiomegalia no desaparecía hasta varias semanas después del tratamiento. De los 4 casos tratados, en uno continuó la mejoría después de suspender el A.C.T.H., en los otros los síntomas reaparecieron, pero a la larga curaron espontaneamente. Fué indudable que hubo una modificación favorable del curso de la enfermedad durante el período terapeútico. La duración total del cuadro varió entre 3 semanas y 3 meses.

Aunque la etiología reumática del padecimiento no puede ser excluída, el diagnóstico diferencial con la pericarditis reumática habitual puede basarse en la actualidad en la ausencia de soplos cardiacos de tipo orgánico, de poliartritis o antecedentes reumáticos personales, la escasa respuesta a la administración de aspirina, la benignidad del proceso, la falta de secuelas cicatriciales endocárdicas y finalmente la ausencia de títulos altos de antihialuronidasa y antiestreptolisinas. Las titulaciones de anticuerpos para los virus de la influenza A y B, linfogranuloma venéreo, psitacosis, fiebre Q, y dos cepas del grupo A y una del B del virus Coxsackie fueron negativas, lo cual no excluye su etiología viral, pero bien podía causarla una hipersensibilidad a distintos alérgenos o que se trate mas bien de un síndrome ocasionado por múltiples factores. Es posible que sea un padecimiento sistémico y que la inflamación fundamental se localice al tejido mesenquimatoso: serosas y músculos.

Como conclusión práctica desde el punto de vista terapeútico los autores afirman que aunque no hubo disminución de la duración de la enfermedad con el uso de los esteroides, pueden ser de utilidad, aunque limitada, especialmente en aquellos casos severos que terminan en insuficiencia cardiaca congestiva.

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TERATOMA OF THE NECK IN A NEWBORN INFANT

Case Report

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TERATOMAS have been described in practically every region of the body. They have been most commonly reported in the ovary, testis, sacro-coccygeal area and mediastinum. Teratoma of the neck has been comparatively rare, having been reported only 60 times. Surgical removal has been attempted in 30 of these 60 patients with presumable cure in 26. Only 3 of the 60 cases reported were found to have malignant tumors. The youngest patient heretofore to have survived removal of a teratoma of the neck was 3 weeks of age.

FIG. 1. Pre-operative A-P view of L neck tumor.
FIG. 2. Pre-operative lateral view of L neck tumor.

CASE REPORT

N. N., a 3 day old, 3.8 kg., white male infant,* was noted at birth to have a large swelling over the left neck. He had been delivered by low forceps after an uneventful pregnancy. He cried spontaneously and was noted to be entirely normal except for a left neck tumor mass. This measured 8.8 cm. by 6.9 cm. by 5.0 cm. When feedings were begun the infant vomited small amounts of each

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* This infant was delivered by Dr. B. Louis Tomaselli and referred by Dr. Edward H. Townsend, Jr., both of Rochester, N.Y.

FIG. 3. Gross specimen of tumor mass in cross section.

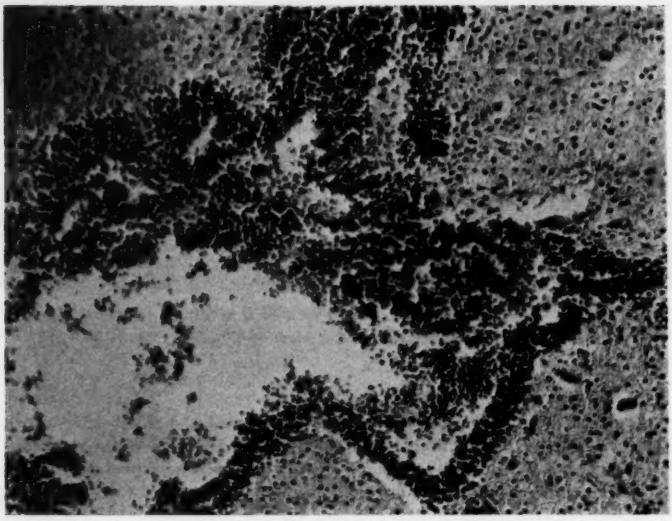

FIG. 4. Nervous tissue. Dark-staining cells are medulloblasts. Light-staining periphery is glial tissue.

feeding. By the third day of life it was believed that the mass had increased considerably in size and was beginning to interfere with respirations.

Physical examination at this time revealed a well developed and well nourished infant whose left neck was completely filled by a large tumor mass (Figs 1 and 2). This extended from the region of the left zygoma down to the left clavicle and from just posterior to the left ear forward to just beyond the midline of the neck. The left ear was pushed upwards by the mass and the infant's mouth was somewhat distorted. The head was pushed slightly to the right. There were several large dilated veins visible in the skin overlying the tumor. The infant was in obvious respiratory distress although no cyanosis was present. On palpation the mass felt cystic. The exact outlines of the tumor were vague and the mass appeared to transilluminate light well.

Laboratory Findings: The examination of the blood showed RBC 5.8 million/cmm., Hgb. 21.7 gm./100 cc., WBC 5.1 thousand/cmm. The differential count was 46% neutrophils, 10% eosinophils, 38% lymphocytes and 6% monocytes. Blood grouping was Type A and Rh factor positive. Fluoroscopy of the neck and chest showed that the soft tissue density was apparently confined to the neck and did not extend down into the thoracic cage. The heart, lungs and diaphragm were normal in appearance. Roentgenograms showed a large homogeneous soft tissue density in the left side of the neck which extended anteriorly. In the upper portion the trachea appeared to be displaced slightly anteriorly and to the right.

The preoperative diagnosis was cystic hygroma. In view of the rapid growth and beginning respiratory embarrassment, plans for immediate operation were made. A polyethylene catheter was placed in an ankle vein and the patient was transferred to the operating room.

Operation: Under intratracheal cyclo-propane-ether anesthesia, the patient was placed with his head turned toward the right side. The entire left face, neck and upper chest were prepared and draped. A transverse elliptic incision was made across the center of the tumor mass. Bleeders were clamped and tied with 5 zero silk. The tumor appeared well encapsulated and was freed fairly easily by sharp and blunt dissection. It extended deep in the neck and was loosely adherent to the major vessels and nerves, to the left submaxillary gland and to the larynx. The mass was firmly adherent to the trachea and could be separated from this structure only by sharp dissection. The left lobe of the thyroid and thyroid isthmus were not visualized. When the tumor was completely freed, it was removed with immediate improvement in the infant's respirations. The wound was then closed in one layer with interrupted 5 zero silks. A dry sterile dressing was applied and the patient was returned to the ward in good condition. Postoperatively 80 cc. of whole blood were given intravenously, followed by a slow 5% glucose in saline drip. The patient was also given 50,000 units of aqueous penicillin every 3 hr. and vitamin K 10 mg. intramuscularly.

Pathologic Report

Gross Description: The specimen removed at operation was a 7.5 x 6 x 2.5 cm. fibrous tumor which was slightly fluctuant. On cut section (Fig. 3) the mass was found to consist of multilocular spaces separated by soft, thick, yellowish fibrous walls. The tissue was slightly hemorrhagic, and the free surfaces had a smooth, shiny appearance. The soft tissue was very friable. The spaces contained small amounts of clear straw-colored fluid.

Microscopic Description: The greatest part of the tissue was composed of various nervous elements (Fig. 4). In predominance were cells having small round nuclei and clear cytoplasm with numerous tiny fibrils forming a network between the cells, obscuring the cell boundaries. These were histologically like neuroglial elements of brain tissue. There was an island of small dark cells with abortive rosette formation reminiscent of the medulloblasts, forerunner of the neuron. There was tissue resembling early meninges with darkly staining psammoma bodies like those seen in meningiomas. A region of darkly pigmented cells, based on their arrangement and location amid brain tissue, resembled early choroid of the eye.

There was fairly well-differentiated thyroid tissue (Fig 5) both near the edge and well within the tumor. Other types of tissue identifiable were: stratified squamous epithelium both in solid sheets and lining cystic spaces (Fig. 6); glandlike structures lined with ciliated cells resembling respiratory epithelium (Fig. 7); fibrous tissue; and blood vessels. These tissues were an admixture of adult and embryonic forms, but each followed an orderly arrangement and the tumor falls into the category of benign teratomas.

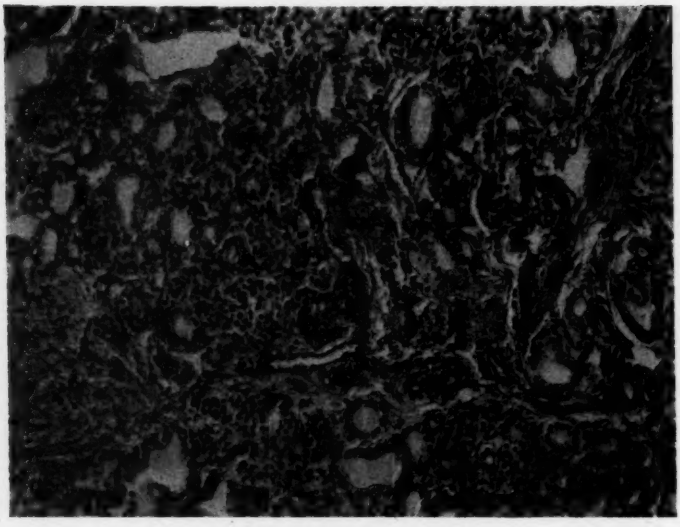

FIG. 5. Well differentiated thyroid tissue.

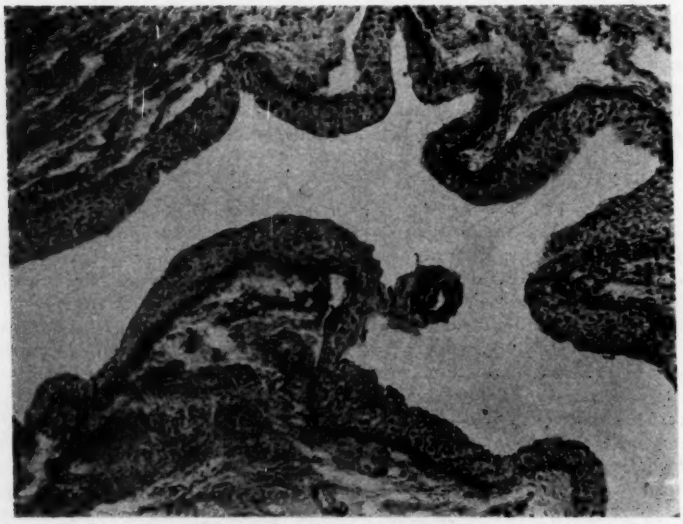

FIG. 6. Cystic cavity lined with stratified squamous epithelium.

FIG. 7. Ciliated epithelium, probably respiratory epithelium.

FIG. 8. A-P view 7 mo. following operation.

Postoperative Course: The patient's postoperative course was satisfactory except for some rhonchi and coarse rales in both lung fields during the 1st 2 days following operation. Sutures were removed on the seventh postoperative day and the baby was discharged home on the eleventh postoperative day. He was last seen 7 mo. after operation at which time he was doing well and had a good cosmetic result (Fig. 8).

Discussion

Tumors of the neck suggestive of teratoma have been reported as far back as 1691, but the first proved case of teratoma of the neck was published by Hess[1] in 1854. Detailed knowledge of the early cases is lacking and in many instances the tumor was observed in stillborns. Bale,[2] in a thorough review of the literature, recently collected 56 authenticated cases and added four additional cases not previously published. These 60 cases are grouped according to their anatomic relationship to the thyroid gland as follows: (1) those tumors supplied by the inferior and/or superior thyroid arteries, the true teratomas of the thyroid gland (8 cases); (2) those tumors not supplied by the thyroid vessels, which displace all or part of the thyroid, the teratomas in the region of the thyroid gland (38 cases); and (3) those tumors not supplied by the thyroid vessels and not displacing any part of the thyroid gland but considered probably in the region of the thyroid gland because of their location and appearance (14 cases). This case would seem to fall into the second group, a teratoma in the region of the thyroid gland. The most common tissues found in these tumors have been brain tissue and thyroid tissue. It is the authors' belief that the patient is the youngest yet reported to have survived surgery for this condition.

Summary

The case history of a three day old infant with a huge teratoma of the neck, endangering the infant's life and demanding immediate surgical attack, is presented. This report illustrates still another condition amenable to operative relief at an early age.

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Spanish Abstract

Teratoma del Cuello en el Recien Nacido; Presentación de un Caso

Los teratomas se han descrito prácticamente en todas las regiones del cuerpo; mas frecuentemente en los ovarios, testículos, area sacro-coccigea y mediastino.

El teratoma del cuello es comparativamente raro; se han reportado únicamente 60 casos. La extirpación quirúrgica se ha intentado en 30, con curación probable en 26. Unicamente 3 de los 60 casos fueron tumores malignos. El paciente mas joven que anteriormente había sobrevivido a la extirpación de un teratoma del cuello era de 3 semanas de edad.

Presentación del caso

N.N. de 3 días de edad, 8 libras y 7 onzas, de sexo masculino, presentó al nacimiento una tumoración grande sobre el lado izquierdo del cuello. El parto fué por aplicación de fórceps bajo y el embarazo fué normal. Lloró espontáneamente y excepto por la masa tumoral del cuello no presentó ninguna otra anomalia. La tumoración media 3½ pulgadas por 2¾ pulgadas por 2 pulgadas. Cuando se inició la alimentación el niño vomitó pequeñas cantidades con todos los alimentos. En el tercer día de vida parecía haber crecido la tumoración considerablemente y comenzaba a dificultar la respiración.

El examen físico en este momento mostró a un niño bien desarrollado y bien nutrido con el lado izquierdo del cuello ocupado por una masa tumoral que se extendía desde la región del cigoma izquierdo hasta la clavícula izquierda y desde atrás de la oreja izquierda hasta un poco mas allá de la línea media del cuello. La oreja izquierda estaba desviada hacia arriba por la tumoración y la boca ligeramente distorcionada. La cabeza estaba inclinada hacia la derecha. Había vasos grandes, dilatados, visibles sobre la piel que recubría el tumor. El niño se encontraba con dificultad respiratoria aunque sin cianosis. A la palpación la tumoración daba una sensación quística. Se transiluminaba con facilidad.

La fluoroscopía del cuello y del tórax mostró que el tejido blando tumoral estaba aparentemente limitado al cuello y no se extendía a la cavidad torácica. Las radiografías mostraron una densidad homogena producida por tejido blando en el lado izquierdo del cuello, apareciendo la traquea en la porción superior, ligeramente desplazada hacia adelante y hacia la derecha.

Bajo anestesia intratraqueal con ciclo-propano eter se trazó una incisión transversal elíptica por el centro de la tumoración. Esta apareció bien encapsulada liberándose fácilimente y observándose que se extendía profundamente en el cuello y que estaba ligeramente adherida a los grandes vasos y nervios, a glándula submaxilar y a la laringe. La tumoración se encontraba firmemente unida a la traquea. Cuando el tumor se extirpó se presentó una mejoría inmediata en la respiración del niño.

El examen histopatológico demostró que se trataba de un teratoma benigno.

El curso post-operatorio fué satisfactorio.

Los 60 casos reportados en la literatura pueden ser agrupados de acuerdo con su relación con la glándula tiroides en la forma siguiente:

(1) aquellos que reciben la circulación de las arterias tiroides inferiores y/o superiores (8 casos); (2) los que no están irrigados por los vasos tiroides y movilizan todo o parte del tiroides (38 casos); y (3) aquellos que no estan irrigados por los vasos tiroides y que no desplazan la glándula tiroides (14 casos). Los autores opinan que el presente enfermo cae dentro de la categoría del grupo segundo, o sea un teratoma en la región de la glándula tiroides. En su opinión es este paciente el de menor edad que se ha reportado y que ha sobrevivido a la intervención quirúrgica.

277 *Alexander Street*

EFFECTS OF PENICILLIN AND BROAD-SPECTRUM ANTIBIOTICS ON THE EMERGENCE OF A GRAM-NEGATIVE BACILLARY FLORA IN THE UPPER RESPIRATORY TRACT OF INFANTS

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THE administration of chemotherapeutic and antibiotic compounds may result in significant changes of the normal microbial flora of the upper respiratory tract; as shown by several investigators.[1-7] This alteration may make it possible for certain microorganisms (monilia, gram-negative, aerobic bacilli, such as E. coli, A. aerogenes, Ps. aeruginosa, etc.) to establish themselves or to propagate profusely. It is this emergence of a new flora which occasionally may be responsible for the development of a new infection. Superinfections of this type have been reported by Weinstein,[8] Appelbaum and Leff,[9] Sommer and Favour,[10] Woods, Manning and Patterson,[11] as well as by Haffner, Neter and Rubin.[6] In infants the emergence of a gram-negative, bacillary flora in the upper respiratory tract has been observed rather frequently following the use of penicillin. The question arises whether this change of the flora can be prevented by the concurrent use of antibiotics effective against gram-negative bacilli. This report summarizes the observations on the emergence of a gram-negative, bacillary, respiratory flora in infants treated with either penicillin alone, or penicillin and a broad-spectrum antibiotic, or a broad-spectrum antibiotic alone. Such a study was deemed of interest, since the emergence of a gram-negative, bacillary flora may have undesirable clinical effects in infants and measures for its prevention would be of practical value.

METHODS

This study was carried out on infants under 2 yr. of age suffering from respiratory infections and other diseases. Nasopharyngeal and throat cultures were taken prior to, concomitant with, and subsequent to, antibiotic therapy. The nasopharyngeal swab was inserted into the nostril and kept in contact with the posterior nasopharyngeal wall for approximately 30 sec. The material from the nasopharynx and the throat was seeded on (1) blood agar, (2) Endo agar and (3) into brain-heart infusion broth. Following incubation of the broth for 24 hr. subcultures were made on Endo agar. The organisms isolated were then identified. The clinical course of the disease was gauged as described in a previous publication.[6]

A total of 107 infants was studied: 12 received penicillin alone; 22 were treated with penicillin as well as a broad-spectrum antibiotic (aureomycin, chloromycetin or terramycin); 21 patients received one of the broad-spectrum antibiotics; 52 infants served as controls and did not receive antibiotic therapy. The data obtained were analyzed statistically.

RESULTS

The incidence of the emergence of a gram-negative, bacillary flora in these four groups of infants is summarized in table 1. It may be noted that this change in the

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TABLE 1

INCIDENCE OF EMERGENCE OF GRAM-NEGATIVE, AEROBIC, BACILLARY FLORA OF UPPER RESPIRATORY TRACT IN RELATION TO TYPE OF TREATMENT

Prior Treatment	No. of Cases with Change of Flora	Total No. of Cases
None	9	52
Penicillin Alone	4	12
Penicillin in Combination with Broad-Spectrum Antibiotic*	15	22
Broad-Spectrum Antibiotic* Alone	4	21

* Aureomycin, chloromycetin and/or terramycin.

bacterial flora took place in a far greater proportion of cases treated with both penicillin and a broad-spectrum antibiotic than in the untreated patients or the infants who received the broad-spectrum antibiotic alone. These differences are statistically significant. The group of patients treated with penicillin alone is too small for definitive conclusions; however, it was previously shown[6] on a larger number of infants that penicillin aids in the emergence of such a gram-negative, bacillary, aerobic flora.

The micro-organisms which emerged or increased in number in the upper respiratory tract were as follows: E. coli, A. aerogenes group: 30 cases; Pr. ammoniae and related species: 3 cases; Ps. aeruginosa: 2 cases; Paracolobactrum: 1 case; and mixture of these micro-organisms: 4 cases.

It seemed of interest to determine whether the emergence of the gram-negative, bacillary flora following use of penicillin was related to the presence or absence of respiratory infection. Of the 107 infants, 71 suffered from respiratory infection (tonsillitis, bronchitis, bronchopneumonia and pneumonia) and 36 from other diseases (intussusception, diarrhea, eczema, etc.). As may be seen from table 2, there was no statistically significant difference between the two groups.

That the emergence of a predominant gram-negative, bacillary flora in the upper respiratory tract of infants may occasionally be significant in aggravating the illness, was previously shown by Haffner, Neter and Rubin.[6] Table 3 summarizes the data on the relationship between this alteration of the flora to reappearance of clinical illness and fever. It may be noted that of 19 infants treated with penicillin or penicillin and a broad-

TABLE 2

INCIDENCE OF EMERGENCE OF GRAM-NEGATIVE, AEROBIC, BACILLARY FLORA OF UPPER RESPIRATORY TRACT IN RELATION TO TYPE OF ILLNESS

Total No. of Cases Studied —107
Total No. of Cases with Change of Flora — 32

Original Disease	No. of Cases with Change of Flora	Total No. of Cases
Respiratory Infections	18	71
Other Diseases	14	36

TABLE 3

RELATION OF EMERGENCE OF GRAM-NEGATIVE, AEROBIC, BACILLARY FLORA OF UPPER RESPIRATORY TRACT TO ILLNESS

Drug(s) Used	Total No. of Cases	Total No. of Patients with Change of Flora	Reappearance of Fever with Change of Flora	Reappearance of Clinical Illness with Change of Flora
None	52	9	3	3
Penicillin	12	4	1	2
Penicillin and broad-spectrum antibiotics	22	15	3	4
Broad-spectrum antibiotic	21	4	0	0
Total:	107	32	7	9

spectrum antibiotic six manifested clinical illness at the time of this change of the flora, whereas none of the four patients treated with a broad-spectrum antibiotic alone did so. Analysis of the available data furthermore revealed that aggravation of illness took place in 8 out of 18 infants whose respiratory flora changed and who originally had suffered from a respiratory infection in contrast to only 1 out of 14 infants whose primary disease was not one of the respiratory tract. It may be concluded, therefore, that the emergence of a gram-negative, bacillary flora of the respiratory tract in infants suffering from respiratory infection may occasionally be associated with reappearance of clinical manifestations. This sequence of events is more frequently encountered following the use of penicillin used alone or in conjunction with a broad-spectrum antibiotic, than with a broad-spectrum antibiotic alone.

DISCUSSION

The data presented in this communication confirm and extend the observations of Haffner, Neter and Rubin,[6] to the effect that treatment of infants with penicillin may be followed by the emergence or by a marked increase in the number of gram-negative, aerobic bacilli in the upper respiratory tract. In the previous study it was shown that such a change of the flora took place even when penicillin was used in conjunction with sulfonamides. From the data presented here it is clear that the emergence of such a gram-negative flora was observed also when penicillin was used together with a broad-spectrum antibiotic, such as aureomycin, chloromycetin or terramycin, namely, in 15 out of 22 patients. In contrast, only 4 of 21 patients treated with a broad-spectrum antibiotic alone showed such a change of flora. Whether this statistically significant difference is due to antagonism of the two anti-infectives cannot be stated with certainty and deserves further investigation. The observation that in infants who received a broad-spectrum antibiotic alone the number of gram-negative bacilli in the upper respiratory tract did not substantially increase is paralleled by the finding of Meads and associates[12] to the effect that aureomycin treatment, in contrast to penicillin therapy, was not followed by the emergence of coliform bacilli in the throat of healthy adults. It was also shown in the present study that the emergence of the gram-negative, bacillary flora in the upper respiratory tract may occasionally be associated with reappearance of clinical manifestations; this may be considered as superinfection, as described by Weinstein,[8] Appelbaum

and Leff,[9] Sommer and Favour[10] as well as by Woods and associates.[11] Therefore, should this change of the flora take place in an infant under penicillin therapy whose respiratory tract infection is not improving or is recurring, treatment with a suitable broad-spectrum antibiotic alone may be preferable to the use of penicillin used exclusively or in conjunction with a broad-spectrum antibiotic.

Summary

A study was undertaken on 107 infants to determine the effect of penicillin and broad-spectrum antibiotics (aureomycin, chloromycetin and terramycin), alone and in combination, on the emergence of a predominant gram-negative, bacillary flora of the upper respiratory tract. The following data were obtained:

1. Such a change of the flora took place in 4 out of 12 patients treated with penicillin, 15 out of 22 treated with penicillin and a broad-spectrum antibiotic, and in only 4 out of 21 infants who received a broad-spectrum antibiotic exclusively.

2. Of the 32 cases whose flora had thus changed, members of the E. coli-A. aerogenes group were found in 30 instances, members of the genus Proteus in 3; Ps. aeruginosa in 2; Paracolobactrum in 1; and combinations thereof in four cases.

3. This change of the flora took place in 18 out of 71 infants suffering from respiratory infection and in 14 out of 36 children suffering from other diseases.

4. Reappearance of clinical manifestations was observed in 6 out of 19 patients whose respiratory tract flora changed following the use of penicillin and in none of the four individuals who were treated with a broad-spectrum antibiotic alone. In view of the small number of cases this observation requires confirmation.

5. It is concluded that in infants the use of penicillin used in conjunction with a broad-spectrum antibiotic is followed rather frequently by the emergence in the upper respiratory tract of a predominant gram-negative, bacillary, aerobic flora; such a change occurs less frequently after the use of a broad-spectrum antibiotic alone. The clinical significance of these data is discussed.

Acknowledgment

The authors wish to express their appreciation to Mr. John Neter, Syracuse University, for the statistical analysis of the data.

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SPANISH ABSTRACT

Los Efectos de la Penicilina y Otros Antibióticos Sobre la Produccion de Flora Bacilar Gram-Negativa en el Tracto Respiratorio Superior del Lactante

La administración de compuestos antibióticos y quimioterapéuticos puede resultar en un cambio importante de la flora microbiana normal del tracto respiratorio superior. Esta alteración hace posible que ciertos microorganismos tales como monilia, bacilos aeróbicos gram negativos como E coli-A. aerógenes, pseudomonas aeruginosa, etc., se establezcan o propaguen profusamente. Esta flora ocasionalmente es responsable del desarrollo de una nueva infección. En el lactante la emergencia de flora bacilar gram negativa en el tracto respiratorio superior ha sido observada con bastante frecuencia después del uso de la penicilina. Surge la interrogación sobre si este cambio de flora puede ser evitado por el uso simultáneo de antibióticos efectivos contra los bacilos gram negativo. En el presente artículo se resumen las observaciones de los autores sobre el desarrollo de una flora bacilar gram negativa respiratoria, en los lactantes tratados y sea solamente con penicilina, con penicilina y otro antibiótico como cloromicetina, aureomicina o terramicina o exclusivamente con cualquiera de estos últimos medicamentos.

El trabajo se efectuó en niños menores de 2 años de edad con padecimientos infecciosos respiratorios y con otras enfermedades. Se tomaron cultivos nasofaríngeos y faríngeos antes, durante y después de, la terapeútica antibiótica.

Se estudiaron un total de 107 niños: 12 recibieron penicilina exclusivamente; 22 fueron tratados con penicilina y con aureomicina, cloromicetina o terramicina; 21 pacientes recibieron solamente uno de dichos antibióticos y 52 mas sirvieron de control sin recibir ninguna terapeútica antibiótica. Los resultados obtenidos fueron analizados estadísticamente.

Se observaron cambios en la flora en 4 de los 12 enfermos tratados con penicilina, en 15 de los 22 en que se empleó penicilina y otro antibiótico, y únicamente en 4 de los 21 niños que recibieron el otro tipo de medicamento. Los cambios en la flora tuvieron lugar en 18 de los 71 niños que padecían infecciones respiratorias y en 14 de los 36 que tenían otras enfermedades.

Los microorganismos que emergieron o aumentaron en número en el tracto respiratorio superior fueron: grupo E coli-A. aerógenes, 30 casos; proteus ammoniae y especies relacionadas 3 casos; pseudomonas aeruginosa, 2 casos; paracolobactrum, 1 caso; y combinaciones de estos microorganismos 4 casos. La emergencia de una flora bacilar gram negativa en el tracto respiratorio de los niños con padecimientos infecciosos respiratorios puede ocasionalmente estar asociada con una reaparición de las manifestaciones clínicas, mas frecuentemente cuando se usa penicilina sola o en combinación con otros antibióticos. El hecho de que el número de pacientes en los cuales hubo un cambio de flora sea mayor cuando se utiliza penicilina sola o junto con aureomicina, cloromicetina o terramicina, puede ser debido a antagonismo de los dos medicamentos anti-infecciosos, sin embargo, la comprobación de esta hipótesis requiere mayores observaciones.

La reaparición de los síntomas infecciosos aconteció en 6 de los 19 enfermos tratados con penicilina y cuya flora se modificó, lo que sugiere que en un niño sujeto a terapéutica penicilínica cuya infección respiratoria no mejora o recidiva, deberá preferirse el empleo de cualquiera de los otros antibióticos mencionados en forma aislada a su utilización combinada con la penicilina o a la aplicación exclusiva de esta.

219 Bryant Street

PREMATURE INFANTS IN LATER LIFE

Study of Intelligence and Personality of 22 Premature Infants at Ages 8 to 19 Years

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THE personality and achievement of premature infants in later life has been studied in a group of 22 unselected infants, born between 1930 and 1942, of birth weights up to 1820 gm. Although this is too small a number for statistical value, the results are pertinent, since thus far there has been but meager investigation of the premature infant's psychologic adjustment. As psychometric examinations are notably more reliable above the age of 8 years, this age group was chosen.[1]

Dunham[2] in 1948 quoted articles which dealt mostly with children of 6 years or less of age, concerning the final intelligence of the premature infant. She, in summary, emphasized the need for well-defined and adequately controlled investigation, before higher incidence of nervous traits and disorders in premature infants could be regarded as established. Reardon[3] expressed the question, "what sort of adults do premature infants make?" and also stated that in comparing groups of premature infants with groups of normal newborn infants, total groups must be compared, rather than to exclude from the premature group those with intracranial hemorrhage. Intracranial hemorrhage is one of the greatest hazards of being born prematurely. They further stated that, group for group, premature infants have more mental deficiency than normal infants. This has been the present authors' experience. Hess[4] has given an outstanding report on the prognosis of prematures. He has analyzed 317 living premature infants whose weight at birth was 605 gm. to 1260 gm. Among these were 130 persons 8 years of age or over, many grown up, married, and in the armed forces. A report was given of physical development and mental status with special reference to the eyes, circulatory system, nervous system and skeletal development. Hess rated 163 of the 317 as normal, or superior in physical status (51%), and 204 of 317, normal, or superior in mental development (64%). He found 36 of the 317 with final evidence of central nervous system pathology (11%), 16 with intraocular defects (4%) consisting of 13 with retrolental fibroplasia and 3 with cataracts. Beskow[5] reported on the mental disturbances in 273 premature infants of school age. Six and one-half per cent of them had cerebral hemorrhage, and later had school difficulty. He noted 50% had nervous symptoms.

PHYSICAL STATUS

The height and weight of the group were normal with the exception of three children, one malnourished, one a dwarf and one obese. There were two children with persistent hypothyroidism, one with congenital absence of four tooth buds, one with cryptorchidism, and one with severe structural scoliosis. One infant was born with bilateral keratitis, no etiologic factor having been found. This infant, Number 51, weighed 1400 gm. at birth.

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The mother's Wassermann test and the infant's tuberculin test were negative. At 2 months of age the right cornea cleared and has remained so. At 9 years of age, the vision in the left eye was 20/200 because of the old scar. This was thought to be a nutritional keratitis. The examination of vision by the Snellen chart, and by refraction in some instances, showed 11 of the 22 individuals to have refractive errors which needed correction by glasses. The average age of the group with poor vision was 13.6 years. This seemed like a greater number with visual trouble than would be expected in 22 average children of these ages. It is interpreted as a sign of incomplete development of the refractive mechanism associated with prematurity, and may be a result of it.

Duke-Elder[6] gives a statement of eye growth as follows: "the axial length of the newborn eye averages about 16 mm. and by the age of eight years it has reached its normal dimension of 24 mm." The eye of the premature in later years tends to have too great an axial length, or the lens system too strong, as a minus lens was needed on every child refracted.

An estimate of what number of normal children may be expected to need to wear glasses showed as an upper limit 23.4% at 9 to 11 years of age, and 18% at 12 years.[7]

The group reported here showed 11 of 22 needing glasses, but this is too small a group for generalization. Details of the cases are given in table 1.

Intellectual Aspects

In assessing intelligence the following tests were used: Wechsler-Bellevue Intelligence

TABLE 1

Height, Weight, Refractive Error of Premature Infants, Listed in Order of Age

Case No.	Age at Study	Ht. (cm.)	Wt. (kg.)	OD	OS	
				Visual Error		
10	19	154	69.4	−4.25 20/200	−4.00 20/200	Correction Perfect
11	19	172	58.1	−0.50 20/135	−0.50 20/68	Correction Perfect
13	18	160	51.3	−1.00 20/120	−1.00 20/88	Correction Perfect
22	15	152	47.2	−3.50 20/200	20/30	Correction Perfect
26	14	166	50.8	20/50	20/50	Correction Perfect
29	14	167	56.7	20/100	20/200	Correction Perfect
35	12	142	27.7	20/50	20/40	Correction Perfect
41	12	149	39.9	−3.25 20/77	−1.25 20/44	Correction Perfect
45	10	144	35.4	20/50	20/44	Correction Perfect
49	9	137	32.2	20/25	20/60	Correction to 20/50 Only
51	8	139	30.4	20/30	20/200	Nebula from Retinitis
5	19	154	47.2	Normal Vision		
6	19	154	41.7			
12	19	162	51.3			
16	17	154	54.4			
17	17	175	70.3			
18	16	172	59.9			
25	15	175	65.3			
31	14	170	61.2			
48	9	137	41.7			
50	8	127	26.8			
52	8	127	24.5			

TABLE 2

INTELLIGENCE AND BIRTH WEIGHT

Case No.	Test Employed	I.Q.	Birth Wt.
11	W-B	132	1800 gm.
41	S-B	130	1765
13	W-B	120	1575
12	W-B	117	1780
45	S-B	114	1000
26	W-B	113	1760
5	Otis	110	1750
48	WICS	109	1340
10	W-B	105	1532
50	WISC	104	1375
22	W-B	103	1500
31	W-B	100	1400
49	S-B	98	1500
17	W-B	93	1758
16	W-B	90	1500
25	W-B	84	1380
52	WISC	80	1370
51	WISC	80	1400
35	W-B	74	1480
29	W-B	73	1320
18	S-B	56	1720
6	W-B	55	1800

TESTS

S-B Stanford-Binet Intelligence Test, Form L.
W-B Wechsler-Bellevue Intelligence, Form 1.
WISC Wechsler Intelligence Scale for Children.
OTIS Otis Self-Administered Intelligence Test. Higher Examination Form A.

Scale, Form 1: Wechsler Intelligence Scale for Children; Stanford-Binet Intelligence Test Form L, and Otis Self-Administered Intelligence Test, Higher Examination Form A. Somewhat surprisingly for such a small group, the 22 I.Q. scores obtained yield a normal curve. This is shown in table 2. The results show two cases of superior intelligence with I.Q.'s of 130, and 132, two of defective intelligence with I.Q.'s of 55 and 56, and the remainder with I.Q.'s between 70 and 130 with a fair distribution. There are, however, six patients with I.Q.'s of 70 to 80, who have not been able to become independent, and are a constant special care to the parents. Five of the six had extreme complications at delivery, consisting of prolonged cyanosis, the administration of morphine in an attempt to stop labor, degeneration of the umbilical cord, and fetal keratitis. This group, thus, shows eight instances of mental retardation in 22, where the average incidence of an I.Q. of 80 or below is approximately 9%.[8] The probable reason for such retardation is intracranial damage as a result of prematurity. With the exception of organic impairment, however, prematurity itself has neither a beneficial nor harmful long range effect on intelligence. There does not seem to appear in this group any correlation between degree of prematurity and intellectual capacity. This relationship is shown in table 2. Many of these children are started in school before they are intellectually mature enough to profit by the experience. All children are sent to school by law at a certain chronologic age,

TABLE 3

TABLE OF 22 INFANTS WITH BIRTH WEIGHT, AGE OF MOTHER,* CAUSE OF PREMATURITY, ECONOMIC STATUS, FINAL AGE AT EXAMINATION, I.Q. AND PERSONALITY RATING

Case	Sex	Race	Birth wt.	Age of Mother	Cause of Prematurity	Economic Status	I.Q.	Age at Test	Personality Rating
					1000–1250 gm.				
45	Female	C	1000	34	Twins-poly hydramnios	Laborer	114	10 Yr.	D
					1251–1500 gm.				
16	Female	W	1500	?	Spont.	Welfare	90	17 Yr.	D+
22	Female	W	1500	35	Placental disease	Business official	103	14 Yr.	B+
25	Male	W	1380	24	Spont.	Laborer	84	14 Yr.	B−
29	Male	C	1320	23	Spont.	Welfare	73	14 Yr.	C+
31	Female	W	1400	36	Placental disease	Bank official	100	14 Yr.	C
35	Female	W	1480	32	Toxemia	Newspaper official	74	12 Yr.	D
48	Female	W	1340	37	Placental disease	Oil Co. salesman	109	9 Yr.	A
50	Male	W	1375	27	Toxemia	Engineer	104	8 Yr.	E
51	Female	C	1400	24	Spont.	Laborer	80	8 Yr.	A−
52	Male	W	1370	44	Placental disease	Laborer	80	8 Yr.	D+
49	Male	W	1500	20	Placental disease	Business official	98	9 Yr.	C
					1500–1750 gm.				
5	Female	W	1750	?	Spont.	Welfare	110	19 Yr.	C−
10	Female	W	1532	37	Spont.	Business official	105	19 Yr.	C−
13	Female	W	1575	28	Twin	Plant insp.	120	18 Yr.	D
18	Male	W	1720	24	Lobar pneumonia	Machinist	56	16 Yr.	
					1751–1820 gm.				
6	Female	C	1800	42	Twin	Welfare	55	19 Yr.	C−
11	Male	W	1800	23	Spont.	Industry owner	132	19 Yr.	C−
12	Female	W	1780	23	Spont.	Machinist	117	19 Yr.	C−
17	Male	W	1758	40	Spont.	Welfare	93	17 Yr.	C−
26	Female	C	1760	22	Spont.	Welfare	113	14 Yr.	C+
41	Male	W	1765	30	Spont.	Bank official	130	12 Yr.	D

* Reardon[2] suggests age of mothers as a contributing cause of prematurity.
W—white
C—Negro

and in this group even more than in any normal group, many should be delayed for a full year before starting.

Personality Aspects

Although prematurity grossly has no permanent effect on intellectual capacity, it may have an effect on mental efficiency. Several of the children, seemingly because of emotional maladjustment, have difficulty utilizing their abilities. An example of this is Case II, Very High Ability, Poor Personality (see Case Reports). Several tended to be overly conscientious and highly motivated, and obtained grades surprisingly high for their I.Q.'s. In an effort to be objective, the following formal personality tests were used in addition to the histories obtained, and to psychologic interviews with each child: The Brown Personality Inventory for Children and the Bell Personality Adjustment Inventory for Students. It is realized that one of the faults of a personality study is that it does not always assess character. The only test for the high qualities of unselfishness, determination, courage and honesty is a personal acquaintance with the individual. With this minor reservation, the tests are of great value. Case 16 (see Case Reports) illustrates this. The total resultant rating, along with other pertinent data, are shown in table 3. The diversification of the socio-economic status of the group is interesting, and it is to be noted that of the two children given a high, or A personality rating, one is from a welfare family. Also of the two given an above average or B rating, one is from a laborer's family, Case 25, Good Personality, Poor Ability (see Case Reports). One of the 22 persons was not given a personality test because of his low I.Q. Twelve of the remaining 21 obtained a score indicating adjustments below average. As a group their social adjustments seemed to be most affected, 12 being of the passive, submissive type, while 8 received scores indicating they are aggressive. In practically every case the results were corroborated by the parents. Fourteen of the children were considered to have definite feeding disorders in the early months beyond that of a normal child. Walking and talking were slightly retarded. Practically all, however, were toilet-trained at 24 months of age, but 7 still had enuresis at 4 years of age. Other signs of neurotic tendency were 2 cases of nail biting, 2 of habit spasms and one of masturbation.

Five of the 22, because of adjustment difficulties, have been referred to psychologists in the past. One, a girl of 11 years, was referred to the psychologist by one of the staff ophthalmologists, because no physical basis was found for her partial blindness. The eventual diagnosis was conversion hysteria. After a few treatment visits of psychotherapeutic nature and interviews with the mother, this girl's condition improved greatly. She is now 14 years of age, and the results of her Bell Inventory show her total personality to be average.

A boy aged 9 years was referred to the psychologist by one of the staff pediatricians because of inability to get along with his brothers and sisters. He is now 19 years old and a student in good standing at a large state university. Personality test results show his total adjustment to be slightly below average.

A girl, 19 years old, a freshman at a state university, has been under treatment by a psychologist at the Student Health Center. She also had conferences with a psychologist while in high school. Her main difficulty is antagonism toward adults, and it was only with persistence that she could be persuaded to come for psychologic studies.

A boy of 9 years was studied at the Children's Center of Metropolitan Detroit for poor emotional adjustment and accomplishment in school. He was under treatment for one year and was advised to transfer from his regular school to a trade school, where he is now

making a better than average adjustment as evidenced both by personality and achievement test results.

One child, the last of this group of five, at 9 years of age, was simply placed in a school situation where expert psychologists supervised him from day to day for six years. The result was blossoming of his latent mental ability and an average personality growth.

Emotional instability of the premature infant was contributed to by the physical strain of prematurity, by the overprotective attitude of the parents, by the poor physical endowment of the premature infant, and perhaps by the rigid type of immediate postnatal care. The birth itself is necessarily a severe experience, for which the fragile and inelastic organism is not ready. Thirteen of the mothers readily stated they were worried, anxious and overprotective to an excessive degree. This is well illustrated by Case 13, High Ability, Poor Personality (see Case Reports). The minor physical ailments of the children made their adjustment more difficult. Finally the present postnatal care of the premature infant is not in accord with the currently prominent theory, that close physical, and psychologic, relation is needed between the infant and mother, even to the point of placing them in the same room to facilitate fondling and tenderness. Dunham[2] has mentioned that the emotional life of a premature infant has received little attention in the development of methods for hospital care. Jackson[9] stated that in the effort to reduce infant mortality hospital procedures have been developed which have disregarded the basic psychologic needs of mother and child. Spock[10] has expressed the opinion that many of the behavior problems of later infancy and childhood have been traced to the patterns established in the early days and weeks after birth. He stated that feeding problems are among the most common behavior disturbances and, in the neonatal period, are more common in premature babies because of the inverse ratio between the baby's size and the mother's anxiety.

At present these rigid schedules exist and for some time to come, premature infants are going to be cared for in incubators under temperature and humidity control, in oxygen and in hospitals. An ordered schedule will be followed because the infants are so inexpressive that it is the only way known to care for them. They cry very little; in fact, they often fail to run a temperature or even a leukocytosis in the presence of infection. They simply have to be subjected to a routine in order to sustain them until they have more nearly the strength of a normal infant. This group will therefore finally offer some help in determining whether such close physical relation, in the earliest days of life, is necessary. The single outstanding finding in this study is that more responsibility should be placed on the child at an early age, that overprotection and anxiety on the parents' part bring on neurotic traits, that parents should be helped to require more responsible action from their children, especially the premature infants.

Case Reports

Case 11: Very High Ability, Poor Personality.—Boy. Born 10/27/31. Birth wt. 1,800 gm. Mother's age 22. Spontaneous premature labor. Intelligence: Wechsler-Bellevue Scale, Form I. Verbal Scale I.Q. 137. Performance Scale I.Q. 118. Full Scale I.Q. 132. Very superior intelligence. Personality: Bell Inventory total rating C minus. Patient is reserved and retiring. Sucked his thumb frequently until 4 yr. of age and in early years had temper tantrums. Walked at 18 mo., talked at 14 mo. Toilet training complete at 18 mo., but had enuresis until 13 yr. of age. Patient has hay fever and allergic dermatitis. He is oldest of 5 children, is the most maladjusted, has been jealous and ambivalent toward the others. In groups he is withdrawn, and retiring, but occasionally aggressive. He disliked school through the first grade and had to be urged. Patient went to private school from eighth to twelfth grade, and earned a C average. He is taking a prelaw course. At age 7 yr. he was

given psychologic guidance because of poor social and emotional adjustment. Parents are well, both college graduates; the father is a noted industrialist. They were extremely overprotective, isolated the child and wore sterile masks when with him until he was 6 mo. old.

Case 16: Low Average Ability, Poor Personality, Great Accomplishment.—Girl. Born 8/26/33. Birth wt. 1,500 gm. Mother's age 30 (?). Spontaneous premature labor. Intelligence: Wechsler-Bellevue Scale, Form I. Verbal Scale I.Q. 86, Performance Scale 95. Full Scale I.Q. 90. Low average intelligence. Personality: Bell Inventory total rating, D+. Patient is second of 3 girls and gets along well with sisters. Her emotional adjustment is poor; in groups she is withdrawn. She does now mostly A and B school work. She does not enter extracurricular activities or clubs. She is in the eleventh grade, and has never had a mark below B, and works extremely hard. She has always been on the honor roll in spite of the estimate of her intelligence. Mother died when she was 7. Father had a grammar school education in Italy, was an immigrant, and is a laborer. Required welfare aid from time to time.

Case 25: Good Personality, Poor Ability.—Boy. Born 3/6/35. Birth wt. 1,380 gm. Mother's age, 24 yr. Spontaneous premature labor. Intelligence: Wechsler-Bellevue Scale, Form I. Verbal Scale I.Q. 76. Performance Scale I.Q. 96. Full Scale I.Q. 84. Dull-normal intelligence. Personality: Bell Inventory total rating, B minus. During 1st 3 yr. he vomited frequently and severely, and now is a finicky eater. Walked and talked at 24 mo. Toilet training complete at 12 mo. but he had enuresis until 4 yr. old. He plays well with other children. He bites his nails a great deal. He was taken out of regular school at the age of 14 and placed in a trade school, where he is making a better adjustment. Parents living, both went through grammar school. Father is a foreman at a large industrial plant, where he has worked for 18 yr. Mother's attitude relaxed, never overprotective.

Case 13: High Ability, Poor Personality.—Girl. Born 3/26/32. Birth wt. 1,575 gm. Mother's age, 28. Cause of prematurity: twin pregnancy. Intelligence: Wechsler-Bellevue Scale, Form I, Verbal Scale I.Q. 113. Performance Scale I.Q. 120. Full Scale I.Q. 120. Superior Intelligence. Personality: Bell Inventory total rating, D. Results indicate patient's home adjustment is poor, and that she is on the withdrawn side. There were many feeding problems, the primary one being anorexia. Patient is now a finicky eater. Walked at 15 mo., talked at 24 mo. Toilet training complete at 21 mo. Twin brother died of scarlet fever at 4 yr. of age. In groups she is withdrawn and tends to be the group isolate. She had much difficulty adjusting to nursery and primary schools, had frequent nightmares, and was a behavior problem until 10 yr. of age. In grade school she did good work, but received unsatisfactory grades in self-control. She graduated from high school with a B+ average. She was overly-conscientious about her school work, and studied very hard. She did not participate in any extracurricular activities or join any clubs while in school. Since graduation she has been employed at the telephone company as a ticket sorter. The parents are living and well and have a grammar school education. Father has been employed for past 20 yr. at an automobile factory where he sets up jobs on the production line. Mother has been excessively anxious and overprotective.

Summary and Conclusions

Physically: A few physical defects were found consisting of malnourishment, dwarfism, obesity, hypothyroidism, congenital absence of tooth buds, scoliosis and cryptorchidism. One child showed keratitis at birth. Eleven children were hyperopic. The condition of the eyes leads to the conclusion that the eyes of the premature may be frequently defective. Otherwise it is difficult to say that prematurity itself effects the physical growth.

Intellectually: The I.Q.'s of the 22 children studied ranged from two of the high grade moron group, upward, with a fair distribution, to two I.Q.'s in the very superior intelligence group. Prematurity per se seemingly has neither a beneficial nor detrimental effect on intelligence except that a more than average percentage of premature infants suffer intracranial hemorrhage as a result of being born prematurely. In these studies, one was definitely diagnosed as having brain damage at birth, and others were suspected of this damage. This seemingly appears in the I.Q. results with a higher than expected incidence of mild mental retardation. Using birth weight as a criterion there was no relation between the degree of prematurity and the resultant I.Q.

Emotionally: Personality test results in addition to the information gleaned from the psychologic interviews and the histories show that over half have made unsatisfactory or below average personality adjustment. Contributing factors were found including prematurity, overprotection by the parents, and poor physical endowment. Twelve of the 22 had personalities of the submissive passive type. Eight of the 22 showed unusual aggressive tendencies. Other behavior aberrations uncovered were nail biting, two cases of habit spasms and one case of chronic masturbation. It is suggested that study of premature infants who are necessarily deprived of immediate postnatal maternal tenderness may finally offer a basis for assessing the theory that such tenderness is necessary.

Acknowledgments

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Spanish Abstract

Evolucion Posterior de Niños Prematuros

Es de gran interés práctico la evolución que en épocas posteriores de la vida presenta la personalidad y el progreso mental del niño prematuro. Investigando este punto se estudiaron en cuanto a inteligencia y personalidad 22 prematuros que al nacimiento tuvieron un peso de 1.820 gms. o menos. El parto prematuro está asociado frecuentemente con daño intracraneano durante el alumbramiento y a menudo interfiere con el desarrollo mental normal. En esta serie 8 de los 22 niños tenían un coeficiente de inteligencia de 80 o menos. No hubo paralelismo entre el grado de prematurez y el de inteligencia. En los 22 niños las pruebas de personalidad mostraron generalmente un adaptamiento pobre atribuible a multitud de factores causales. Doce de los niños tenían personalidades de tipo sumiso o pasivo. Ocho mostraban tendencias agresivas. Para los 24 meses de edad ya se les había educado a todos en el control diurno de sus esfínteres, pero 7 fueron enuréticos hasta los 4 años. Un niño presentó un defecto ocular marcado. Once de los 22, o sea un 50% tuvieron errores visuales que ameritaban el empleo de anteojos. En un grupo normal, éste tipo de defectos aparecería en solo el 23.4%.

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PRIMARY HERPETIC VULVOVAGINITIS

Report of a Case; Isolation and Identification of Herpes Simplex Virus

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PRIMARY infection with the virus of herpes simplex may cause a variety of clinical entities encountered in pediatric practice. The most common of these diseases, acute herpetic gingivostomatitis,[1-4] can usually be recognized with ease. On the other hand, primary herpetic vulvovaginitis,[5] keratoconjunctivitis,[6,7] meningoencephalitis[8-10] and eczema herpeticum (Kaposi's varicelliform eruption)[11,12] are much rarer conditions which usually require virus isolation and serologic studies to establish a diagnosis of primary infection.

Children with acute herpetic gingivostomatitis are seen frequently in this pediatric clinic. In contrast, herpetic vulvovaginitis has been rare. It seems worth while, therefore, to report the following case which was corroborated by virus isolation and serologic studies.

CASE REPORT

M. A., a 26 mo. old white girl, was seen in the pediatric clinic with a chief complaint of pain on urination. Her illness began 3 days previously when she developed a high fever, anorexia and irritability. Two days before, she complained of pain in the perineal area, and the day prior to entry, her mother noted an eruption on the vulva. The eruption increased in severity and became so painful that the patient refused to void for the 20 hr. period before she was seen in the clinic.

There was no known contact with anyone who had a fever blister. She had never been immunized against diphtheria.

Physical examination revealed an acutely ill, fretful child with a temperature of 38.1°C. and a pulse of 100/min. While being examined, she voided spontaneously with a great deal of pain. On the vulvovaginal area, which was markedly reddened and edematous, there were several superficial shallow ulcers measuring 3 mm. in diameter. The inguinal glands were enlarged and tender bilaterally.

Urinalysis revealed 20 WBC/hpf. Examination of the blood disclosed a WBC count of 8.7 thousand/cmm. with 50% neutrophils, 47% lymphocytes and 3% monocytes. Culture of the vaginal lesions was negative for diphtheria bacilli. Kahn test was negative.

During the 1st 3 days in the hospital, the vaginal lesions became more extensive. Many of the ulcers coalesced forming larger lesions with a grayish white base (Fig. 1).* By the 14th day of the illness, all the lesions had become crusted, and by the 20th day, the perineal and vulvovaginal areas were entirely normal.

VIRUS ISOLATION STUDIES

A swab of the vaginal lesions, which was obtained on the day following admission, was rubbed onto the scarified cornea of a rabbit. A marked keratoconjunctivitis was noted 72 hr. later. The nictitating membrane which was reddened and edematous, was removed under sterile precautions and prepared for chick embryo passage. The rabbit's eye was enucleated for histologic section of the cornea. The microscopic sections revealed the presence of characteristic type A intranuclear inclusion bodies.

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* This photograph of herpetic vulvovaginitis was obtained from another patient whose lesions were similar to those of M.A. in this report.

FIG. 1. Herpetic vulvovaginitis.

A 10% aqueous suspension of the nictitating membrane was treated with penicillin (500 u./cc.) and inoculated in 0.1 cc. amounts onto the chorioallantoic membranes of four 13 day old chick embryos. After incubation for 45 hr. at 36°C., the eggs were iced and harvested. Each membrane contained approximately 100 pinhead sized oval plaques. Grossly, these lesions resembled others produced by a strain of herpes simplex (HF) virus.

Acute and convalescent sera were obtained from the patient on the 8th and 29th day following the onset of illness. Using the chorioallantoic membrane technic,[13] it was possible to demonstrate a rise in neutralizing antibodies against the HF strain of herpes simplex virus (table 1). A constant amount of herpes simplex (HF) virus was mixed with undiluted serum and serum diluted 1:16. The virus-serum mixture after incubation for 90 min. at 4°C. was inoculated onto the chorioallantoic membrane of four 11 day old embryonated eggs. After 40 hr. of incubation, at 36°C. the membranes were removed and the plaques were counted. The presence of neutralizing antibodies was indicated by the absence or reduction of plaques.

A similar test was employed for identification of the agent as herpes simplex virus. A constant

TABLE 1

DEVELOPMENT OF NEUTRALIZING ANTIBODIES TO HERPES SIMPLEX VIRUS (HF strain)

Patient's Serum	Dilution of Sera	
	Undiluted	1–16
Acute phase 3/5/51	55*	42
Convalescent phase 3/26/51	16	0
Control (normal rabbit)	N.T.	60

* Each figure represents the average number of virus plaques on 4 membranes produced by inoculation of a mixture of the serum and known herpes simplex (HF) virus. Absence or reduction of plaques indicates development of neutralizing antibodies.

N.T.—not tested.

TABLE 2

NEUTRALIZATION OF PATIENT'S VIRUS BY HERPES IMMUNE SERA

Serum	Dilution of Sera	
	Undiluted	1–16
Herpes (HF) immune rabbit	0*	0
Control (normal rabbit)	10	28
Patient's acute phase 3/5/51	30	17
Patient's convalescent phase 3/26/51	0	0

* Each figure represents the average number of virus plaques on 4 membranes produced by the inoculation of a mixture of the indicated serum and the patient's virus. Absence of plaques indicates presence of neutralizing antibodies.

amount of the patient's virus* was mixed with the following undiluted and diluted (1:16) sera: (1) patient's acute serum which had been shown to be free of neutralizing antibodies to the HF strain of herpes virus, (2) patient's convalescent serum containing neutralizing antibodies, (3) herpes simplex (HF) immune rabbit serum and (4) negative control or normal rabbit serum. It can be seen in table 2 that the agent was neutralized by both the herpes simplex (HF) immune rabbit serum and the patient's convalescent serum. On the other hand, it was not affected by the normal rabbit serum or by the patient's acute phase serum.

DISCUSSION

The unknown agent had the following characteristics which identified it as herpes simplex virus: (1) it was recovered from a herpetic lesion; (2) it caused a keratoconjunctivitis on the scarified cornea of a rabbit with characteristic type A intranuclear inclusion bodies in the epithelial cells; (3) it produced typical plaques on the chorioallantoic membranes of embryonated eggs; (4) it was neutralized by herpes simplex (HF) immune rabbit serum.

The identification of the virus and the demonstration of the rise of neutralizing antibodies established the patient's disease as a primary herpetic infection. Recurrent herpetic vulvovaginitis differs from this condition in two respects: (1) neutralizing antibodies are present in the same high titer during both the acute and convalescent period and (2) there is an absence of constitutional symptoms.

Diphtheritic vulvovaginitis may be confused with herpetic infection because the grayish white base of several coalesced ulcers may simulate a membrane. Therefore, material from the lesions should be cultured on a Loeffler's serum agar slant. Other conditions to be considered in the differential diagnosis include impetigo, ammoniacal dermatitis and accidental vaccination with vaccinia virus.

The treatment of herpetic vulvovaginitis is entirely symptomatic. Antibiotics do not alter the natural course of the disease and are not indicated in the absence of secondary infection. Local applications of nupercaine ointment may alleviate some of the pain caused by the superficial erosions.

* 10% aqueous suspension of infected nictitating membrane.

SUMMARY

A case of primary herpetic vulvovaginitis is reported. This diagnosis was confirmed by isolation of the virus and demonstration of the development of neutralizing antibodies.

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SPANISH ABSTRACT

Vulvovaginitis Herpética Primaria

Se describe un caso de vulvovaginitis herpética primaria. Este padecimiento, en contraste con la gingivoestomatitis herpética aguda, es relativamente raro. El diagnóstico se estableció por los siguientes datos: 1.—presencia de lesiones herpéticas en el area vulvovaginal asociadas con síntomas generales; 2.—identificación del agente, a partir de las lesiones, como el virus del herpes simple; y 3.—demostración de una alza en los anticuerpos neutralizantes para la cepa HF del virus del herpes simple, durante la convalescencia.

477 First Avenue

COMPARATIVE TOXICITY OF AQUEOUS AND OILY PREPARATIONS OF VITAMIN A

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A PREVIOUS study[1] by the authors reported that the absorption and storage of vitamin A is inversely proportional to the particle size of its vehicle of administration. Thus superior absorption and storage followed the administration of experimental doses of vitamin A in aqueous preparations, which are of microscopic particle size, when compared with the administration of comparable unitage in the oily products, which are of macroscopic particle size. This effect of the particle size of the vehicle, amply corroborated, appears common to all the fat soluble vitamins and in retrospect explains the reported observations of the influence of the menstruum of administration on the antirachitic effectiveness of vitamin D,[2] on the blood levels,[3-7] storage[6] and excretion[6] of vitamin A, and as more recently shown[8] on the absorption curve of vitamin E. The observations on vitamin A were the result of studies in man and in the laboratory animal following administration of experimental doses large enough to effect significant blood rises, liver storage and excretion. Recently Ellingson[9] confirmed these observations of liver storage in the rat but reported no difference in the absorption and storage of aqueous and oily preparations of vitamin A when administered in low and therapeutic dosage.

In view of the increasing awareness and incidence of clinical hypervitaminosis A,[10,11] it seemed worth while to investigate whether administration of excessive amounts of the aqueous preparations of this vitamin would result in greater toxicity, due to its superior absorption, when compared with like amounts of the oily product. It was necessary by the very nature of the study to pursue this problem in the laboratory animal. The resulting data should, however, have some pertinence clinically inasmuch as the previous experience indicated that rats responded to oily and aqueous preparations of vitamin A in much the same manner as humans.

The effects of vitamin A poisoning in the rat have been investigated by many workers since the early reports of Takahashi.[12] Rodahl,[13] in a recent comprehensive monograph, found the manifestations of toxicity to include reduced growth, hemorrhagic diathesis, alopecia, inflammatory changes of the periorbital tissues, exophthalmos and spontaneous fractures. In all previously reported toxicity experiments in the rat, vitamin A was administered in an oily menstruum. For the purpose of this study percentage mortality and spontaneous fracture rate were the objective criteria of comparison.

EXPERIMENTAL PROCEDURES

Three groups of 100 adult male rats weighing 175 to 200 gm. were fed at different dose levels,

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* Deceased.

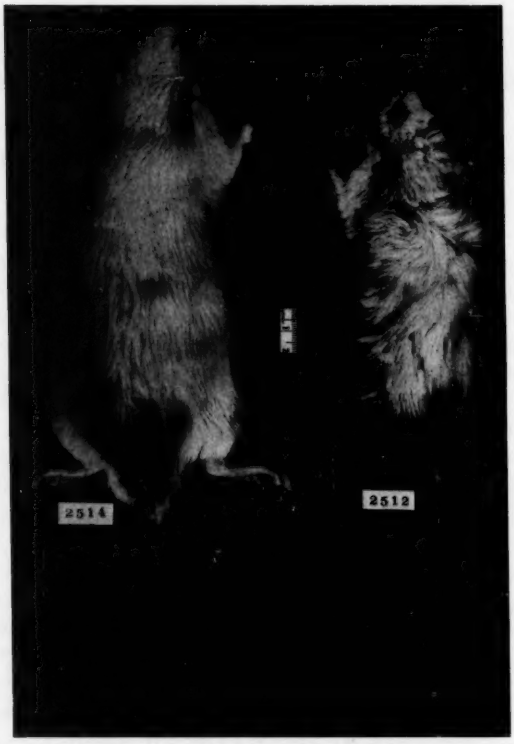

FIG. 1. A. Control animal. B. Rat fed 100,000 i.u. vitamin A in aqueous preparation daily for 8 days. Note loss of weight, scruffiness of pelt, swelling of orbital area.

comparable amounts of an aqueous* and oily† preparation of vitamin A daily for 21 days in the following manner:

Group 1.	A. (50 rats) 25,000 i.u., aqueous B. (50 rats) 25,000 i.u., oily
Group 2.	A. (50 rats) 50,000 i.u., aqueous B. (50 rats) 50,000 i.u., oily
Group 3.	A. (50 rats) 100,000 i.u., aqueous B. (50 rats) 100,000 i.u., oily

The daily volume of the oily and aqueous preparation in each group was kept constant by diluting the oily preparation with cottonseed oil and both preparations were fed by stomach tube. Each animal was examined daily for signs of toxicity. RGs were made every fourth day. At the end of the 21 day period blood was taken from the heart of the survivors in each group 48 hr. after the last feeding to determine the level of vitamin A in the blood. At the time of bleeding the animal was killed to ascertain the amount of vitamin A stored in the liver. To rule out the possible toxic effect of the vitamin A vehicle in each group 20 animals were fed equivalent amounts of cottonseed oil as a control for the oily preparation and similarly 20 animals were fed, as controls, equivalent amounts of the diluent solution used in the preparation of the aqueous vitamin A product. The vitamin A assays were done by the methods described in a previous investigation.[11]

* Aquasol (50,000 i.u. vitamin A/cc.), U.S. Vitamin Corp.

† Vitamin A concentrate, natural esters (200,000 i.u./cc.), Distillation Products.

Results

Clinical effects of poisoning were evident by the second to the third day in the group receiving 100,000 i.u. of the aqueous preparation daily. The animals became sluggish, the hair ragged, diarrhea was common and there was a marked loss of appetite and weight as compared to the control animals (Fig. 1). Deaths began to occur on the third day and by the eighth day all animals had succumbed to vitamin A poisoning. In marked contrast, as may be seen in chart 1, the group receiving 100,000 i.u. of the oily preparation daily suffered a mortality rate of only 5% during this same period. At the 50,000 dose level, the results, though not as striking, were similar: A mortality of 8% with the aqueous preparation, and of 2% with the oily product. It is noteworthy that at the end of the first week the mortality rate of the 50,000 i.u. aqueous group was comparable to that of the group fed twice this amount of vitamin A in an oily vehicle. The relative toxicity of the aqueous and oily preparations persisted to the end of the 21 day experimental period (chart 1) at which time there was a 17% mortality rate in the 100,000 i.u. oily group as compared to a 40% mortality in the group being fed half this amount daily in

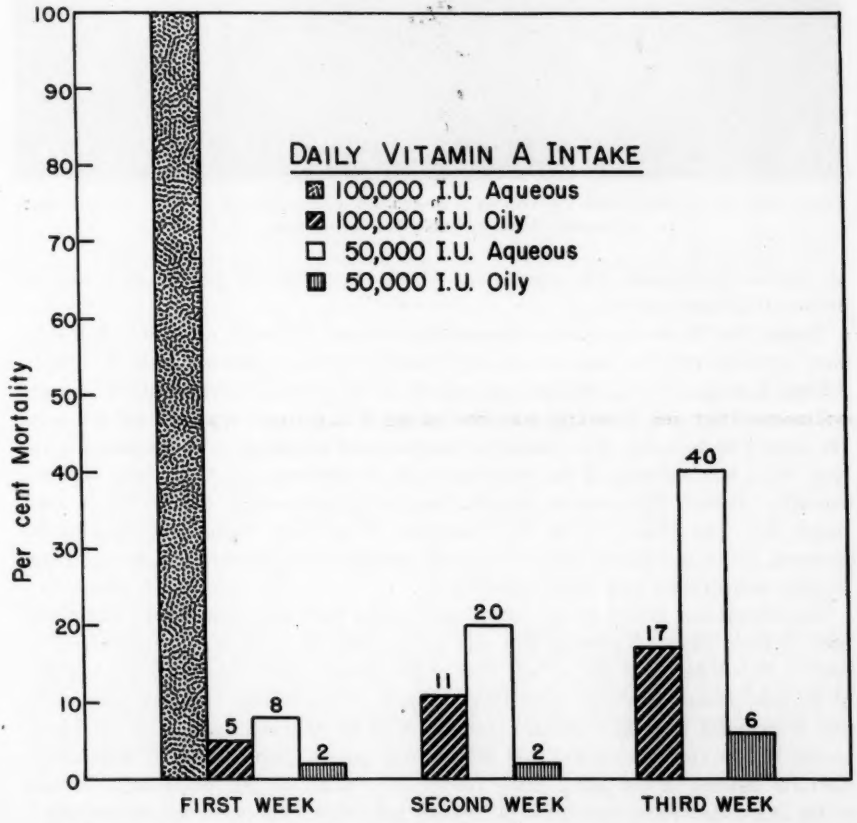

Chart 1. Mortality rate in rats following administration of excessive amounts of aqueous and oily preparations of vitamin A.

FIG. 2. RGs of rats fed 50,000 i.u. vitamin A in aqueous media daily for 16 days. Note fractures of humerus, femur and tibia. Marked scoliosis in A.

an aqueous menstruum. The animals fed 50,000 i.u. of the oily product daily suffered an over-all mortality of 6%.

During the 21 day experimental period the observed symptoms of vitamin A toxicity were: scruffiness of the pelts, drowsiness, muscular weakness, bleeding, lack of appetite, reduced growth, alopecia, swelling and redness of the palpebrae, exophthalmos, limping and spontaneous fractures. Limping was first noted in the hind legs and did not occur till the 8th to 10th day. RGs revealed a narrowing of the diameter of the shafts of the long bones with thinning of the cortex especially at the metaphysis. The bones appeared normally calcified. Spontaneous fractures were seen beginning at the twelfth to fourteenth day. The fibula was the most common site of early fracture followed by the humerus, femur and tibia in that order. Gross scoliosis of the vertebral column was noted in many animals after the second week (Fig. 2).

The comparative incidence and rate of spontaneous fractures following the administration of toxic doses of aqueous and oily preparations of vitamin A are illustrated in table 1. It will be noted that a daily dose of the aqueous preparation only one half that of the oily product produced comparable numbers of spontaneous fractures. Thus at the end of the third week RGs revealed fractures in 45 of 50 animals and 38 of 50 animals in the 50,000 i.u. aqueous and 100,000 i.u. oily groups, respectively. Six spontaneous fractures resulted in the group being fed 50,000 i.u. of the oily preparation. In view of the fact, as previously noted, that all animals fed 100,000 i.u. of the aqueous vitamin A died within 8 days, there is no comparable data on spontaneous fractures in this group.

TABLE 1

INCIDENCE OF SPONTANEOUS FRACTURES IN RATS FOLLOWING ADMINISTRATION OF EXCESSIVE AMOUNTS OF AQUEOUS AND OILY PREPARATIONS OF VITAMIN A

No. of Animals	Vitamin A Intake Daily for 21 Days	No. of Animals with Spontaneous Fractures
50	50,000 i.u. Aqueous	45
50	50,000 i.u. Oily	6
50	100,000 i.u. Oily	38

Liver storage and postabsorptive vitamin A blood levels in the various dosage groups are recorded in table 2. Control animals were fed 13,500 i.u. daily for 21 days. Liver storage at this dosage was comparable to results obtained in the authors' previous report[6] following a single test dose. Storage is complicated by the fact that excessive intake of vitamin A causes toxic liver damage; it is nevertheless apparent from table 2 that liver storage is markedly decreased in both the aqueous and oily groups following toxic doses. It is also noteworthy that the decrease in storage is greater in the livers of animals fed the aqueous preparations than in those fed the oily product. Thus though the normal animal will store 54% following administration of 13,500 i.u. from an aqueous menstruum, the toxic animal being fed 50,000 i.u. of an aqueous preparation will store only 8%. The decrease following the oily product in the same dose range is from 39% in the normal animal to 12% in the toxic animal.

TABLE 2

POSTABSORPTIVE BLOOD LEVELS AND PER CENT LIVER STORAGE IN RATS FOLLOWING INCREASING INTAKE OF AQUEOUS AND OILY PREPARATIONS OF VITAMIN A

Vitamin A Intake Daily for 21 Days	Postabsorptive Blood Level (units/100 cc. Plasma)		Per Cent Total Intake Stored in Liver	
	Aqueous	Oily	Aqueous	Oily
13,500 i.u.	117 (32)*	111 (32)	54%	39%
25,000 i.u.	190 (11)	153 (11)	10%	18%
50,000 i.u.	573 (21)	200 (21)	8%	12%
100,000 i.u. (intake for 5 days)	1,663 (9)	511 (21)	6%	10%

* Number of animals.

In view of the consistent finding[13, 15] of fatty degeneration of the livers in rats fed excessive amounts of vitamin A, it is not improbable to assume from the data seen in table 2 that the liver damage resulting from vitamin A poisoning decreases storage of the vitamin and thus adds to the increased blood levels and tissue saturation of vitamin A when taken in toxic doses.

DISCUSSION

Distinction has been made between "acute" and "chronic" vitamin A poisoning in the animal as well as in man. The acute syndrome as observed in the group of animals

fed 100,000 i.u. of the aqueous preparation daily is characterized by weakness, loss of appetite, diarrhea, scruffiness of the pelt and marked loss of weight within one to two days. Rodahl and Moore[16] have reported a similar syndrome in the Eskimo manifested by drowsiness, irritability, headache, vomiting and desquamative dermatitis following ingestion of polar bear or bearded seal liver, a pound of which was found to contain 1,000,000 i.u. vitamin A. The liver of the Greenland fox, long known by the Eskimo to be poisonous, was also found to be rich in vitamin A. Though there are no reports of "acute" vitamin A intoxication in the pediatric literature, chronic poisoning is now a recognized entity occurring usually in infants over 9 months of age following daily intake of excessive amounts of vitamin A (100,000 to 500,000 i.u. daily) for periods of several months to years. Outstanding symptoms of hypervitaminosis A reported in the pediatric age group include lack of appetite, irritability, lassitude, pruritus, loss of hair, hepatomegaly, splenomegaly, anemia, pain and swelling usually of the soft tissues along the bones of the extremities and reluctance and inability to use the affected part. RGs of the involved bones reveal varying degrees of periosteal elevation and surrounding soft tissue reaction. The similarity of the roentgenographic findings in hypervitaminosis A with those of infantile cortical hyperostosis has been reported by Caffey.[17] In the present authors' limited experience with three cases of infantile cortical hyperostosis, vitamin A blood studies were normal.

There are no postmortem reports of vitamin A poisoning in man. In the rat microscopic pathologic findings include[13]: generalized hyperemia, vascular extravasation, degeneration of the renal tubules, fatty degeneration of the liver cells, massive cutaneous hemorrhages around the root sheaths of the hair and subperiosteal and osseous hemorrhages, destruction of bone spicules, thinning of the compact bone and an increased number of osteoclasts. In spite of the spontaneous fractures and disorganized bone structure, there is no change in the calcium or phosphorus content of bone ash as compared with the normal animal. The spontaneous fractures produced in adult rats in these experiments with excessive vitamin A intake are in agreement with the observations of Rodahl[13] and contrary to the findings recorded by Moore[18] and others[19] who reported fractures occurring primarily in the growing bones of the young animal.

Little is known of the mechanism of vitamin A toxicity. From the data in the authors' experiments as well as the experience of others, it is believed that the liver is first saturated with vitamin A following excessive intake. With liver saturation continued intake results in increased blood levels, tissue saturation and liver damage, which further decreases the ability of the liver to store the vitamin. It is the continued saturation of liver and bone with large amounts of vitamin A that probably effects the toxic changes. Thus, in the animal, fractures do not occur until two or more weeks of ingestion of toxic doses; in the infant and child symptoms are evident usually after months of excessive intake of vitamin A. The vitamin A saturation and impaired function of the liver may be inferred by the fact that in the infant and child a period of weeks to months may intervene between the time of cessation of vitamin A intake and return to normal blood levels.

Whether the effect on bone and bone growth of vitamin A toxicity was due indirectly to a disturbed mineral metabolism or to a direct effect of the vitamin on bone and cartilage has been uncertain. In a recent outstanding contribution, Fell and Mellanby[20] have established the fact that the effect of a high concentration of vitamin A on developing bone tissue is a direct one. By growing the bones of fetal mice in tissue culture they studied the effects of altering the concentration of vitamin A in the media. They found: "the

control bones in normal media did not lengthen much during cultivation but deposition and absorption of bone continued in vitro . . . the effect of the vitamin A acetate on the experimental bone was remarkable. In a concentration of 2,000-4,000 i.u. per ml the soft tissue grew as richly as in the controls, but in three days the bone of the shaft began to be absorbed and the cartilagenous ends to soften and shrink. The process progressed rapidly and the entire bone rudiment seemed to melt away like a 'lump of sugar in hot water': in extreme cases by the tenth day only a few crumbs of bone were left scattered in the sheet of actively growing soft tissue. . . . Histological sections of the experimental bones showed that the cartilage matrix soon lost its basophilia and at the same time shrank, while the cells appeared normal. Finally the matrix of the epiphyses vanished completely, leaving only a compact mass of chondroblasts, while the diaphysial cartilage was rapidly invaded and replaced by the highly cellular connective tissue of the marrow cavity. Exactly how the bone was absorbed was not clear, and although osteoclasts were fairly numerous it was doubtful whether they accounted for all the destruction." Although one hesitates to transpose results of in vitro and animal experiments to human physiology, these observations of Mellanby and Fell are striking enough to suggest that the bone pathology of hypervitaminosis A is due to the direct action of high concentrations of the vitamin on cartilage and bone.

It is therefore apparent that in man as in the animal repeated doses of excessive amounts of vitamin A are not without harmful effect. Since, as demonstrated in this report, aqueous preparations of vitamin A are more toxic in the rat than comparable amounts of the oily product, it is probable that in man a similar ratio will pertain. In view of the fact that clinical hypovitaminosis A is rarely seen in pediatric practice and since the minimum requirement in this age group is usually met in the normal diet, there seems to be little need for prescribing vitamin supplements which contain excessive amounts of vitamin A especially if dispersed in an aqueous menstruum.

Summary

Vitamin A toxicity in the rat as manifested by mortality rate and incidence of spontaneous fractures was greater following the administration of excessive amounts of vitamin A in an aqueous menstruum as compared to a similar intake of the vitamin in an oily vehicle.

Liver damage, due to vitamin A toxicity, impaired the ability of the liver to store the vitamin. Ingestion of toxic doses of the aqueous preparation resulted in greater depression of liver storage than comparable amounts of the oily product.

The mechanism of vitamin A toxicity is discussed.

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SPANISH ABSTRACT

Toxicidad Comparativa de las Preparaciones Acuosas y en Aceite de la Vitamina A

La toxicidad de la vitamina A, que en las ratas se manifiesta por un aumento de la mortalidad y de la incidencia de fracturas espontáneas, fué mayor después de la administración de una cantidad excesiva de vitamina A en un medio acuoso, comparada con una ingestión similar de dicha vitamina en un vehículo aceitoso.

La lesión hepática, por toxicidad a la vitamina A, dificultó la habilidad del hígado para alamacenar esta vitamina. La ingestión de dosis tóxicas en forma ácuosa provoca una mayor disminución en el almacenamiento hepático de la vitamina A que cuando se emplean cantidades comparables del producto en aceite.

Se discute el mecanismo de toxicidad de la vitamina A.

8 Gramercy Park

SALMONELLA BREDENEY MENINGITIS

Case Report of a 19 Day Old Infant

By HOWARD L. KANTOR, M.D.
Brooklyn

SALMONELLA infection, particularly Salmonella meningitis, was considered a fatal disease less than 14 years ago. In 1937 Bahrenburg and Ecker[1] reported 32 known fatal cases of Salmonella meningitis out of a total of 35 cases. The review of these cases revealed the inadequacy of bacteriologic and therapeutic aids available at that time. Progress made in the next decade is statistically supported by Henderson,[2] who, 11 years later, concluded that the survival rate of Salmonella meningitis had markedly increased. Closer examination of these 147 cases of Salmonella meningitis reviewed by Henderson reveals, however, no instance of recovery of a newborn infant with this disease. Of 49 cases of Salmonella meningitis in an age group less than one month, only one case, aged 23 days, recovered.

A case of Salmonella bredeney meningitis with recovery in a 19 day old infant is reported. This is the youngest infant with Salmonella meningitis of any type in which there was a recovery. No cases of Salmonella bredeney meningitis have been reported in the literature.

REPORT OF CASE

A 3 wk. old white male infant was admitted to the Brooklyn Jewish Hospital with a 24 hr. history of anorexia and unresponsiveness. The infant had a weak cry, was apathetic, and had refused to take feedings for a 24 hr. period prior to admission. A temperature of 38.8°C. was noted 2 hr. before admission which prompted the parents to seek medical attention.

This infant was the product of a normal spontaneous full term delivery born to a para 0, gravida 0 mother following an uneventful prenatal course. Birth weight was 3030 gm. The infant was normal at birth and the neonatal course in the hospital was uneventful. The patient was discharged at 7 days of age. The 1st 2 days at home were marked by a mild diarrhea consisting of 6 to 8 watery yellow stools daily. A formula of evaporated milk 1:1 with 5% dextrimaltose was changed to evaporated milk 1:2 with 5% dextrimaltose mixture following which the diarrhea abated. For the next 10 days this infant thrived, weighing 4550 gm. at the onset of the present illness 24 hr. before admission.

Family history was noncontributory.

Physical examination on admission revealed a pale listless infant appearing acutely ill. There was a shrill high-pitched cry noted periodically during the examination. Temperature was 39.2°C., pulse 105/min., respiration 30/ min. The skin was pale, clear, well hydrated. A right parieto-occipital cephalohematoma was noted which did not appear inflamed. Anterior fontanel was 2 x 2 cm., tense and bulging. The eyes presented a stare. No nuchal rigidity, Kernig or Brudzinski's signs were found. A Moro reflex could not be demonstrated although all other reflexes, both superficial and deep, appeared physiologic. The chest and abdomen were negative as were the ears, nose and throat. Bacterial meningitis was suspected and substantiated by the initial laboratory data. These data revealed Hgb. 76%; WBC count 28 thousand/cmm., with polymorphonuclears 31%, band forms 35%, lymphocytes 30%, monocytes 4%. On lumbar puncture 8 cc. of milky opalescent fluid were obtained under increased cerebrospinal fluid pressure. Microscopic examination revealed 2,500 cells predominantly polymorphonuclear leucocytes, while chemical examination showed a low spinal fluid sugar and an elevated spinal fluid protein (see table 1).

Direct smear of the spinal fluid sediment revealed a gram-negative bacillus. A blood culture was

From the Department of Pediatrics of the Jewish Hospital of Brooklyn.
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TABLE 1

SUMMARY OF CEREBROSPINAL FLUID DATA

Date	Amount	C.S.F. Pressure	Appearance	Microscopic	Chemical Determinations	Bacteriology
6/25	5 cc.	Increased	Milky	2,565 cells 85% polymorphs 15% lymphocytes	sugar—25 mg./100 cc. prot.—240 mg./100 cc.	gram-neg. bacillus smear-pos. culture Salmonella
6/26	12 cc.	Subnormal	Green	14,240 cells 95% polymorphs	sugar—29 mg./100 cc. prot.—491 mg./100 cc.	gram-neg. bacillus smear-pos. culture Salmonella
6/27	3 cc.	Subnormal	Sanguinous	4,000 cells 65% polymorphs	sugar—21 mg./100 cc. prot.—544 mg./100 cc.	negative culture
6/28	4 cc.	Markedly subnormal	Turbid	2,000 cells 50% polymorphs	sugar—20 mg./100 cc. prot.—491 mg./100 cc.	negative culture
7/8	6 cc.	Normal	Clear	115 lymphs	sugar—43 mg./100 cc. prot.—93 mg./100 cc.	negative culture
7/12	6 cc.	Normal	Clear	22 lymphs	sugar—60 mg./100 cc. prot.—68.8 mg./100 cc.	negative culture

drawn and combined intrathecal and parenteral therapy were begun immediately, although the organism had not definitely been identified.

For the 1st 4 days this infant received daily lumbar taps followed each time by the instillation of streptomycin 25 mg. and aqueous penicillin 10,000 units intrathecally. For the 1st 8 days of illness streptomycin 50 mg./kg. in 24 hr. and a 5% solution of Na sulfadiazine subcutaneously in 0.065 gm./lb. in 24 hr. dosage were administered. Aureomycin 50 mg./kg. in 24 hr. was given orally until the third day when, because of several loose stools, this was discontinued and oral chloromycetin in the same dosage was substituted.

On the second hospital day, the child developed tremors of all the extremities, a left facial spasm, a temperature spiking to 40.0°C., a dusky pallor, and a generally fulminating toxic state. Oxygen was administered and a transfusion of 80 cc. whole blood (10 cc./lb.) was injected into a scalp vein as a supplement to chemotherapy and antibiotics. Lumbar puncture on the second day revealed a greenish-yellow opalescent fluid under subnormal cerebrospinal fluid pressure. There were 14,000 cells predominantly polymorphonuclear leucocytes, with a persistently low sugar and a rising cerebrospinal fluid protein level. Again the spinal fluid smear showed a gram-negative motile rod.

Forty-eight hours after admission the laboratory reported the successful culture of a Salmonella organism. Positive spinal fluid cultures of this organism were grown with ease from the specimens of the first and second lumbar taps only. The initial blood culture was also positive for the same Salmonella organism. Repeated daily blood cultures for 3 days after initiating therapy were negative. Repeated urine and stool culture samples failed to reveal the Salmonella organism. Serum agglutinins on admission revealed a Typhoid H, d titre of 1:80. Specific serum agglutination studies for Salmonella bredeney, although not done on admission, were negative in 5 days and again in 2 wk. Sensitivity tests indicated the organism was inhibited by 6 γ/cc. of both streptomycin and chloromycetin and by 8 γ/cc. of terramycin. It was tolerated by 10 γ/cc. of aureomycin. The sulfa level in the serum was consistently between 8 to 12 mg./100 cc.

Agglutination studies with serum of B group identified this organism as belonging to the B group. A specimen of the culture was sent to the New York Salmonella Center. The organism was identified there by Dr. Erich Seligman as Salmonella bredeney.

The third day the child was decidedly improved clinically. The fontanel was no longer tense or bulging, the pallor had disappeared, and temperature returned to 37.0°C. The next 2 taps on days 3 and 4 were mechanically difficult since apparently a lumbar block had occurred. However, fluid collected from lumbar taps on these days were cultured. Report of negative spinal fluid cultures and decreased cell counts found in these specimens prompted the author to withhold further lumbar taps and, with this, all intrathecal therapy was discontinued on the fourth hospital day.

On the 14th hospital day lumbar puncture showed clear fluid under normal pressure with 115 cells, slightly low sugar and elevated protein. On the 17th hospital day, a grossly clear spinal fluid was obtained which proved to be normal on microscopic and chemical examination.

From the third day on, the child was asymptomatic, afebrile, gained weight, and thrived as a normal healthy infant. The child went on to an uneventful recovery.

On the eighth day streptomycin and penicillin therapy were discontinued. On the tenth day, the infecting organism was found to be inhibited in undiluted serum and up to a titre of 1:8. Sulfadiazine was discontinued on the 15th day and chloromycetin on the 17th day. The infant was discharged on the 22nd hospital day.

On the day that a Salmonella organism was positively identified, a careful review of the public health aspect of the history revealed the following significant facts concerning the family history:

One and a half months before delivery of the patient, both parents along with almost every guest at a mountain resort hotel were stricken with an acute onset of diarrhea, nausea, malaise and generalized muscular aches and pains unassociated with fever or vomiting. After 2 days on symptomatic treatment both parents recovered and experienced no sequelae from this brief episode. The diarrhea was said to have been caused by "spoiled water."

Bacteriologic studies of both father and mother revealed: enteric agglutinins Typhoid H, d. 1:80 in mother, negative in father. Salmonella bredeney agglutination was negative in the mother. Stool cultures were negative in both parents. The Board of Health laboratories also found stool cultures to be negative for Salmonella organisms in both parents.

A follow-up on the patient indicated that at 3 mo., the weight was 5.9 kg., the child held its head up, began to sit with assistance, was alert, and followed light adequately. Apparently the infant had made a complete recovery without sequelae. Further follow-up was unobtainable.

Comment

In the latter half of the 19th century, Smith and Salmon first isolated the organism causing salmonellosis, then considered a disease of the gastrointestinal tract. Today there are more than 160 species of the Salmonella organism known, which may be found invading any tissue of the body. Although Salmonella bredeney is a member of group B, it is more characteristic to find group C Salmonella organisms causing such extraintestinal lesions as meningitis.

In newborn infants, as pointed out by Cooke and Bell,[3] there is a combination of low permeability of the intestinal mucosa, low resistance to bacterial infection, and a predilection to infection following the trauma of birth. Bornstein[4] noted that when this site of predilection of Salmonella infection in newborn infants was to the meninges, it was the result of a locus minoris resistentiae. The presence of a cephalohematoma in the patient is evidence of the trauma of delivery and possibly represents a locus minoris resistentiae. Although infections of different etiology may reportedly precede a Salmonella infection, none was discovered in this case. Henderson[2] noted that meningococcal meningitis preceded the discovery of Salmonella meningitis in five cases he reviewed from the literature.

Pediatricians are well aware that neonatal infections in general often present an elusive clinical picture with a paucity of signs and symptoms. Meningitis in particular, occurring in the neonatal period, is notorious for the absence of the classical signs of meningeal irritation, for absence of hyperpyrexia, and for its rapidly fatal course. The fortunate early appearance of hyperpyrexia was the only observation that urged the parents of this patient to seek early medical attention. Yet in less than 36 hours from the onset of symptoms, a bulging fontanel, grayish cyanosis, and a high pitched cerebral cry were evident clinically.

When purulent spinal fluid was obtained, a multiplicity of antibiotics were administered and a sulfonamide drug was empirically introduced until the organism was cultured and its sensitivity tested toward the therapeutic agents used. The desirability of repeated

lumbar taps may be open to question. The author thought the indications were two: prognostic and therapeutic. Prognostically, it was possible to judge the result of the therapy. Therapeutically relief of the increased intracranial pressure and high antibiotic spinal fluid levels were achieved. The organism was found sensitive to streptomycin at a level of only 6 γ/cc. indicating a relatively resistant organism. The author feels confident, therefore, that the favorable and prompt clinical response of the patient was due to early and effective antibiotic levels obtained in the spinal fluid. Intrathecal administration of streptomycin was considered instrumental in sterilization of the spinal fluid by the third hospital day and the favorable and prompt clinical response that ensued.

Another interesting feature of this case was the marked and immediate clinical improvement noted following transfusion. Not only was the cyanosis and skin coloring improved, but also the facial spasms and tremors disappeared, and the child reacted from its shocklike state. Blood transfusions are well known as an excellent supportive measure in overwhelming infections. Transfusions of whole blood are particularly emphasized in the literature as having a dramatic therapeutic effect in salmonellosis. Henderson[2] considered this measure as important a factor as antibiotics in the recovery of one case reported from his study. The frequency of transfusions and their benefit were noted in other cases in his review.

Because of reported resistance to therapy and the frequent relapses due to latent foci of infection in Salmonella meningitis reported by Schweig et al. in 1947,[5] chloromycetin, an effective agent against Salmonella, was not discontinued until the 17th day when the spinal fluid was found to be clear and sterile. The author feels confident that the complete recovery noted three months later was due to prolonged antibiotic therapy far beyond what seemed clinically indicated.

The Salmonella organism identified by the laboratory as a member of group B was classified as Salmonella bredeney by the New York Salmonella Center. Seligman[6] stated that this organism may be transmitted to humans through ducks found particularly in sections of Long Island, New York. Subsequent to the identification of this Salmonella as a member of group B, a group having the greatest carrier rate, the family was investigated. Although the recent history of epidemic gastroenteritis which affected both parents was obtained, neither was found harboring the organism.

Summary

A case of Salmonella bredeney meningitis with recovery in a 19 day old infant is reported. This is the youngest patient with Salmonella meningitis known to have recovered. This is the second known case of Salmonella meningitis with recovery in a patient less than one month of age. Treatment with multiple antibiotics and chemotherapy both parenterally and intrathecally produced rapid improvement. An equally effective supportive blood transfusion may have aided this recovery. The use of chloromycetin after discontinuance of all other antibiotics was effective in producing a clinical recovery without relapse. No sequelae were noted at the end of a three month observation period.

Attempts at discovering the carrier state of the infesting organism by careful examination of the family revealed no source of infection.

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SPANISH ABSTRACT

Meningitis por Salmonella Bredeney; Un caso en niño de 19 días de edad

La importancia de este caso reside en que es el primero curado en tan temprana edad que ha sido reportado.

El lactante fué admitido con historia de 24 horas de apatía, anorexia y temperatura de 102 grados por las dos horas previas a su admisión en el hospital. Los antecedentes de parto y neonatales no fueron de significación. La exploración física dió como datos positivos, además de la fiebre, cianosis, con tinte grisáseo, abombamiento de la fontanela y grito cerebral, sin ningun otro síntoma de irritación meníngea. La punción lumbar reveló líquido cerebroespinal purulento cuyo cultivo y el de la sangre fueron positivos para la salmonela bredeney.

La predilección de la infección meníngea en esta edad esta probablemente condicionada por la escasa permeabilidad de la mucosa intestinal, la poca resistencia a la infección y la predisposición producida por el traumatismo del nacimiento. Efectivamente, se ha demostrado que cuando la infección se localiza en las meninges es el resultado de una resistencia local disminuída como sucedió en este enfermo afecto de cefalohematoma. En ocasiones se han encontrado infecciones de diferente etiología previa a la infección pero en este caso no las hubo.

El diagnóstico temprano es uno de los factores fundamentales de éxito terapeútico, desgraciadamente es de observación frecuente la notoria ausencia en el recíen nacido de los signos clásicos de irritación meníngea, hiperpirexia y su curso rápidamente fatal.

En este caso en particular los autores del artículo aseguran que la terapeútica temprana con diferentes antibióticos por vía parenteral e intratecal, sulfas, los niveles efectivos obtenidos en el líquido cefalorraquídeo, las transfusiones frecuentes de sangre total y la prolongación de la cloromicetina durante 17 días después de haber suspendido los otros antibióticos cuando el líquido espinal ya era claro y estéril, fueron factores fundamentales para que el niño tuviera una recuperación completa, sin recaída, y que tres meses después no tuviera secuela alguna.

Es de importancia enfatizar lo ya citado por otro autor acerca de los resultados terapeúticos dramáticos obtenidos por transfusiones de sangre total en las salmonelosis considerándolas aun tan importantes como la terapeútica antibiótica misma. No pudo localizarse la fuente de la infección.

555 Prospect Place

RETROLENTAL FIBROPLASIA: ANIMAL STUDIES

Induced Vascular Engorgement and Hyperplasia of the Iris, Tunica Vasculosa Lentis and Retina in Kittens

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TERRY[1] in 1942 first named retrolental fibroplasia and related the disease to prematurity. The incidence of blindness associated with prematurity has increased remarkably since then, and this increase is due to retrolental fibroplasia alone.[2] The incidence of the disease in infants born weighing less than 1.3 kg. varies from zero in some nurseries to over 60% in others.[2-5] The common range of incidence of permanent blindness varies from 8 to 20% in infants born weighing less than 1.3 kg.

Although much has been learned of the histology[1,3,4,6,7] and pathogenesis[4,6,7] of the disease, the etiology is not known. Inability to produce retrolental fibroplasia in animals has made investigation of the disease difficult.

This article reports the results of an attempt to produce retrolental fibroplasia in kittens.

METHOD

Twelve litters of kittens were used. Beginning the second day of life, half of each litter of newborn kittens was given intraperitoneal infusions of 0.9% saline equal to 10% of the body weight twice daily. Pitressin tannate in oil, 0.2 to 0.5 cc., was given by injection twice daily. Some of the kittens in each group so treated had swelling of the paws and eyelids. When this swelling was well established, massive transfusions of the mother's blood were given intravenously rapidly until gasping and cyanosis were evident. These transfusions were repeated twice weekly, for periods ranging from 13 to 43 days. Repeated ophthalmoscopic examinations were made of the eyes of all the kittens, control and experimental, at twice weekly intervals. The kittens were killed in pairs, control and experimental, for histologic examination of the eyes.

The swelling of the feet and eyelids was capricious, the omission of a single infusion of saline or injection of pitressin allowing the accumulated fluid to disappear. The transfusions were occasionally fatal, the cause of death being massive pulmonary edema.

RESULTS

Edema was produced and maintained by the method used in 18 members of six of these litters. Seven kittens died of pulmonary edema due to the massive transfusions; 5 were not transfused; 6 experimental and 7 control animals survived to be killed.

The time of opening of the eyes was from 7 to 10 days after birth. At the time of opening of the eyes all kittens had fine remnants of the anterior part of the tunica vasculosa lentis, and an easily visualized hyaloid system and posterior portion of the tunica vasculosa lentis. All remnants of the embryonic vascular supply of the lens disappeared by

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Work done at the University of Chicago in the laboratories of the Division of Ophthalmology, Department of Surgery, University of Chicago.

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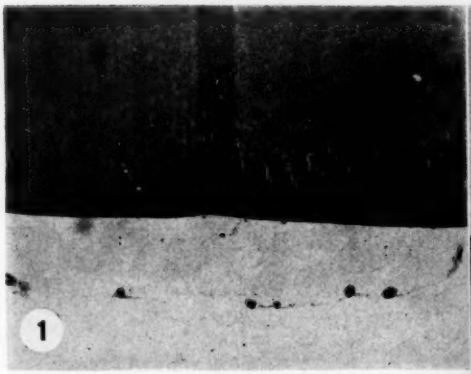

FIG. 1. Capillary network of posterior part of tunica vasculosa lentis (32 days).

FIG. 2. Budding of vessels from iris to form anterior portion of tunica vasculosa lentis (43 days).

the 21st day in the control kittens. In the edematous kittens in which the transfusions were not done, the embryonic vascular system could not be made to persist, and unequivocal vascular engorgement of the retinal vessels was not found. In the edematous transfused kittens, the embryonic vascular systems, the radiating vessels of the irides, and the retinal vessels were severely dilated following each transfusion for several hours, and remained mildly so between transfusions.

These six litters were killed at intervals from age 13 days to age 43 days, and the eyes of each litter were fixed and sectioned for histologic examination. The eyes of the 13 day old control kitten had the complete remnants of the embryonic vascular system. However, the vessel walls were thick and the lumens were small, in comparison with the hyaloid system and anterior and posterior parts of the tunica vasculosa lentis of the

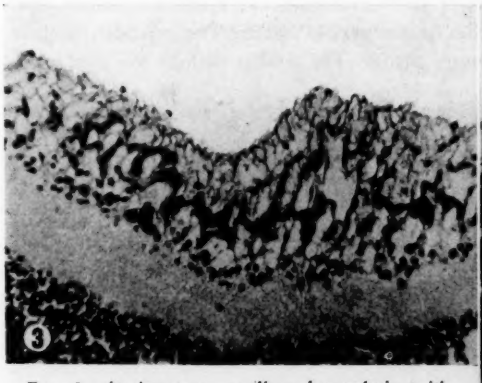

FIG. 3. Angiomatous capillary hyperplasia with chronic inflammatory cell infiltration in thickened inner layers of retina (32 days).

FIG. 4. Retina of control kitten (28 days) of same litter as Fig. 5.

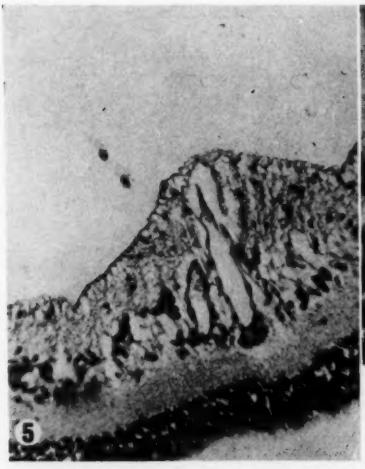

FIG. 5. "Basket" formation with thickened inner layers of retina and mild inflammatory infiltrate (28 days).

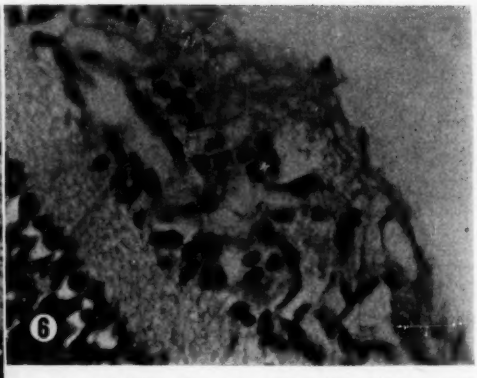

FIG. 6. High power view of capillary whorl. Blood cells are easily seen in tortuous vessels, as are chronic inflammatory cells around vessels (32 days).

transfused edematous kitten. In the 23 day old litter, no fetal vascular system remained in the control. However, the test animal had a widely patent hyaloid artery and vascular network behind the lens (Fig. 1). Large vessels arose from the iris anteriorly, and traversed the pupil giving off numerous branches to form the anterior network of the tunica vasculosa lentis (Fig. 2). The retinal blood vessels were dilated, and halfway between the ora serrata and the optic nerve several clumps of capillary angiomatous networks were seen confined under the internal surface of the retina (Figs. 3-6). In these regions the internal layer of the retina bulged toward the vitreous. Evidence of a mild chronic inflammatory cell infiltration was seen in some of the sections from these regions. The periorbital vessels are greater in size and number in the treated animals (Figs. 7 and 8). The vitreous humors of the test animals had sparsely scattered white cells, particularly near the large branches of the hyaloid system. The anterior chambers, however, had no evidence of inflammatory change. The same pathology was seen in the

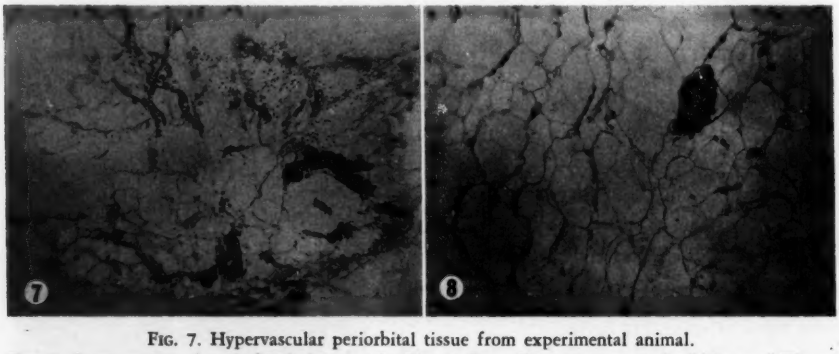

FIG. 7. Hypervascular periorbital tissue from experimental animal.
FIG. 8. Same region of periorbital tissue as in Fig. 7. From litter mate control of kitten of Fig. 7.

remainder of the litters, including the 43 day old litter, with variations in degree of change, but not in essential description.

Discussion

Filling the extracellular fluid spaces to the point of edema and then repeatedly administering massive blood transfusions maintains the embryonic vascular supply of the lens. The hyaloid system and the budding iridal vessels are dilated and engorged with blood. The tunica vasculosa lentis remains intact in its entirety to the 43rd day of life, if edema is maintained and massive blood transfusions are repeatedly given. Neither the edema alone, nor transfusion alone could, in the author's hands, maintain these structures.

The retinal changes, however, are of more immediate clinical interest. Reese and Blodi[6] describe the histologic changes in the eyes of an infant who weighed 1400 gm. at birth and died at the age of 11 weeks, after early retrolental fibroplasia had been identified clinically. Angiomatous tissue extends from the retina into the vitreous in the periphery of the retina, which has a mild inflammatory cell infiltration. The retinae have dilated blood vessels, as do the choroids and orbital tissue sections. The iridal blood vessels are also dilated in their patient. However, no remnants of the embryonic vascular system are found in their patient. Heath describes the histologic changes seen at birth in the eyes of a 1600 gm. infant.[7] He believes that these changes represent the early reversible stage of retrolental fibroplasia. His sections are strikingly similar to the sections of the kittens. (See Figs. 6 and 7 in reference 7, and Fig. 3, this article.) At histologic examination the test kittens have capillary angioma-like structures with mild surrounding inflammatory cell infiltrations in the periphery of the retinae. However, these vessels are not seen to enter the vitreous. The retinae in the regions of the angioma-like networks bulge toward the vitreous, but no point of break through the internal limiting membrane of the retina could be identified. Engorgement of the retinal vessels is more easily seen in the live animal than in the histologic studies, although it is easily identified in the latter.

Although great similarity of histopathology exists between these animal studies and some human studies, final conclusions about the similarity of etiology cannot be made. The data are offered as a possible clue for further investigations in the premature infant.

Summary

A condition similar to the early retinal stages of retrolental fibroplasia, along with persistence of the ocular embryonic vascular system, is induced by repeated massive blood transfusions of chronically edematous kittens.

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SPANISH ABSTRACT

Fibroplasia Retrolental: Estudios en Animales

La fibroplasia retrolental fué por primera vez descrita y correlacionada con la prematurez en 1942. La incidencia de ceguera asociada a la prematurez ha aumentado notablemente desde entonces y este aumento es debido exclusivamente a la fibroplasia retrolental. La frecuencia de la enfermedad en niños con peso menor de 1.360 grms. varía desde cero en algunas instituciones hasta mas del 60% en otras. La etiología del padecimiento es desconocida y la dificultad para producir fibroplasia retrolental en animales ha dificultado la investigación del padecimiento.

Este artículo describe los resultados de un intento para producir fibroplasia retrolental en gatitos.

Se utilizaron 12 camadas de gatitos. A partir del segundo día de vida a la mitad de cada camada se les administró intraperitonealmente, 2 veces al día, una solución salina al 0.9% igual a la décima parte del peso corporal. También dos veces al día se les aplicó tanato de pitresín en aceite, 0.2 a 0.5 c.c. Algunos de los gatitos de cada grupo tratados en esta forma presentaron edema palpebral y de las zarpas. Cuando se estableció edema franco se aplicaron transfusiones masivas rápidas de sangre materna hasta presentarse cianosis y disnea. Esas transfusiones se repitieron dos veces por semana, por períodos que variaron desde 13 hasta 43 días. Los gatitos fueron sacrificados por pares, uno del grupo de control y otro del grupo experimental.

Se produjo y se mantuvo el edema por el método descrito, en 18 miembros de 6 de las camadas. Siete gatitos murieron de edema pulmonar por las transfusiones; 5 no fueron transfundidos; sobrevivieron para ser sacrificados 6 del grupo experimental y 7 animales del grupo de control.

En los gatos utilizados como control los restos de la circulación vascular del cristalino desaparecieron para el veintiunavo día. En los gatos edematosos que no fueron transfundidos, no persistió el sistema vascular embriónico ni se encontró claramente congestión vascular de los vasos retinianos. En los gatitos edematosos transfundidos se observó por varias horas después de cada transfusión, que el sistema vascular embriónico, lo vasos del iris y los vasos retinianos se encontraban francamente dilatados, alteraciones que permanecían, aunque en forma menos acentuada, durante el intervalo entre las transfusiones.

En el examen histológico del ojo de los gatos del grupo control, a los 23 días de edad no se encontró restos del sistema fetal vascular. En cambio, en los animales del grupo experimental había permeabilidad amplia de la arteria hialoide y una red vascular detrás del cristalino. De la parte anterior del iris partían grandes vasos que atravesaban la pupila dando ramas numerosas para formar la red anterior de la túnica vasculosa del cristalino. Los vasos retinianos estaban dilatados y entre la ora serrata y el nervio óptico se encontraron agrupamientos de vasos capilares angiomatosos, confinados a la superficie interna de la retina. En estas regiones la capa interna de la retina hacía prominencia hacia el vitreo. En algunas secciones de estas regiones se encontró evidencia de una infiltración celular crónica inflamatoria leve. Los vasos periorbitarios fueron mayores en tamaño y número. El vitreo presentaba algunos leucocitos dispersos, particularmente cerca de las grandes ramas del sistema hialoide. Sin embargo, no había evidencia de cambios inflamatorios en la cámara anterior.

Aunque hay gran similaridad histopatológica entre estos estudios en animales y algunos en humanos, no pueden exponerse conclusiones definitivas acerca de una etiología similar. Se ofrecen estos datos como una posible pista para investigaciones posteriores en el niño prematuro.

The University of Texas Medical Branch

STUDIES ON ABSORPTION AND DISTRIBUTION OF TERRAMYCIN IN CHILDREN

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TERRAMYCIN is an antibiotic isolated from the elaboration products of the actinomycete, Streptomyes rimosus. It is an amphoteric substance which is rather insoluble in water. Its acid and basic salts, however, are readily soluble in water, and it is the hydrochloride which is available commercially for general use. In aqueous solution, it has a pH of 1.5. Terramycin hydrochloride is very stable, and in aqueous solutions at pH 1.0 to 2.5 there is no detectable loss of activity at room temperature (25° C.) or even at 50° C., over periods of at least 30 days. In the dry state it shows no detectable loss in biologic potency on prolonged storage at room temperature, and even when maintained at 50° C. for 4 months, less than 5% inactivation is observed.[1]

Terramycin and its salts are equally effective so far as antimicrobial action is concerned. The spectrum of activity is wide, and includes the majority of gram-negative and gram-positive organisms of pathogenic potentiality, with the exception of Pr. vulgaris and Ps. aeruginosa. The minimal inhibitory concentration of terramycin for the majority of the susceptible organisms ranges from 0.3 μg./cc. to 5.5 μg./cc.[2] Although S. typhi is inhibited in vitro by the antibiotic, Bauer et al.[3] and Knight[4] have been unable to demonstrate terramycin to be effective in the treatment of clinical typhoid fever. In general, the range of usefulness parallels that of aureomycin and chloramphenicol, with chloramphenicol being definitely the drug of choice in typhoid fever.

Several studies of serum levels in adults have been reported. Schoenbach et al.[5] found the antibiotic to be detectable in the serum within one-half hour after the ingestion of a single 2 gm. dose. Maximal levels of 3.0 to 5.0 μg./cc. were attained 2 to 4 hours later, and concentrations of 0.5 to 1.3 μg./cc. were present 24 hours after ingestion. With a dosage schedule of 500 mg. every 3 to 6 hours, no cumulation of terramycin occurred in the serum, with average levels of 2.0 to 8.0 μg./cc. being obtained. Welch[6] found essentially similar patterns of absorption, with peak levels being attained 2 to 6 hours after ingestion. Single oral doses of 0.25 gm., 0.5 gm., 1.0 gm. and 2.0 gm. gave, respectively, peak levels of approximately 1.8, 1.4, 3.5 and 5 μg./cc. Significant cumulative effect in serum levels did not occur when 0.25 gm., 0.5 gm. and 1.0 gm. were given every six hours after four doses. Herrell et al.[7] gave oral doses ranging from 1.0 to 3.0 gm. to adults and concluded that the serum concentration was not significantly increased by tripling the dose. On single doses, peak levels were reached from 1 to 4 hours after ingestion, were maintained for as long as 10 to 14 hours, and detectable levels in general were no longer present after 24 hours. On multiple doses of 1.0 gm. every six hours there was a tendency

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TABLE 1

SERUM TERRAMYCIN LEVELS

Single Dose—11 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Level μg./cc.—hr. after ingestion			
			2	4	6	8
R. L.	23	250	1.95	1.85	1.4	1.3
P. B.	23	250	1.28	0.76	0.67	0.72
R. J.	17.2	200	1.10	0.66	0.32	0.31
L. C.	20.0	200	1.20	1.4	0.90	0.66
J. K.	17.6	200	0.49	1.14	0.70	0.41
A. J.	50	500	0.40	0.64	0.40	0.32
C. J.	47	500	0.15	0.31	0.15	0.15
J. G.	26	250	0.20	0.15	0.15	0.15
W. M.	4.5	50	0.52	—	0.25	—
D. D.	52	500	0.32	—	0.28	—

for cumulation with serum concentrations reaching, in four cases, 8 μg./cc., and in one case, 16 μg./cc. These workers also determined spinal fluid levels after 1.0 gm. terramycin had been given orally every 6 hours for 24 hours in 6 patients. Serum levels at that time ranged from 4 to 8 μg./cc. In one case the CSF level was 1 μg./cc., while in the others there was virtually no detectable antibiotic activity.

Studies of this nature in children have not been reported. In this study, the authors have attempted to determine serum levels on various dosage schedules, to base dosage on body weight, and to arrive at a rational regimen for the administration of terramycin in pediatric practice.

METHODS

Serum and cerebrospinal fluid terramycin levels were performed by the turbidimetric bioassay method which has previously been described from this laboratory by Whitlock et al.[8] In single dosage studies, the terramycin was administered by one of the authors to convalescent children who were free of renal or cardiac disease. The antibiotic was given at least 2 hr. postprandially. The drug was given either in capsule form or as a powder mixed in corn syrup.

TABLE 2

SERUM TERRAMYCIN LEVELS

Single Oral Dose—22 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Level, μg./cc. at hours			
			2	4	6	8
J. A.	16	350	1.5	1.2	0.73	0.6
L. F.	30	650	2.3	2.0	1.3	0.9
F. G.	54	1200	2.5	2.2	1.23	0.84
D. H.	18	400	0.83	1.5	2.0	1.8
E. P.	30	650	1.5	2.0	1.6	1.6
D. H.	28	600	1.2	0.9	0.6	
J. J.	13.7	300	1.2	1.0	0.6	
R. K.	25	550	0.3	0.2	0.27	
J. M.	14	300	1.3	0.92	1.18	
B. S.	11	250	1.8	1.3	1.18	

TABLE 3

SERUM TERRAMYCIN LEVELS

Single Oral Dose—33 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Level, μg./cc. at hours			
			2	4	6	8
R. T.	12	400	0.8	0.68	0.78	
W. R.	25	850	0.68	0.66	0.68	
I. O.	30	1000	1.1	0.92		
J. P.	17.2	650	2.48	1.9	1.5	
M. B.	19.5	650	0.52	0.75	1.5	
L. B.	16	500	1.6	1.8	1.5	
E. P.	30	1000	1.96	1.2	1.96	0.84
R. M.	18.6	650	0	0.74	2.0	1.2
D. H.	18	600	2.0	1.7	1.5	

RESULTS

Oral Administration: Single oral doses of terramycin 11 mg./kg. body weight were given to 10 patients ranging in weight from 4.5 to 52 kg., and serum levels were obtained at 2, 4, 6 and 8 hours after ingestion. The results are shown in table 1. Peak levels which ranged from 0.20 to 1.95μg./cc. were beginning to decline six hours after ingestion. Excluding the two cases in which four hour levels were not obtained, the mean peak level on this dosage is 1.0 μg./cc. serum.

Twenty-two mg./kg. was given to 10 children ranging in weight from 11 to 54 kg. and the resulting serum levels are revealed in table 2. The pattern of absorption is similar to that seen on the small dosage. Two hour levels are possibly slightly higher, ranging from 0.3 to 2.5 μg./cc. with a mean of 1.43 μg./cc. The four hour levels are essentially identical with the two hour values, with a mean of 1.32 μg./cc.

With a dosage of 33 mg./kg. given to nine patients, the mean two hour level was 1.23

TABLE 4

SERUM TERRAMYCIN LEVELS

Single Oral Dose—66 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Level, μg./cc. at hours			
			2	4	6	8
R. M.	18.6	1200	0.3	0.8	1.2	1.52
J. J.	13.6	900	4.2	4.6	5.0	2.7
L. S.	15	1000	1.28	1.88	2.5	
R. T.	12	800	4.6	5.0	3.7	
J. A.	16	1000	3.8	2.3	2.2	2.2
D. H.	28	1800	0.8	3.0	3.6	3.8
D. H.	18	1200	1.2	2.6	2.9	3.0
E. P.	30	2000	2.8	1.64	1.64	
F. G.	54	3500	2.4	2.8	2.4	
E. W.	9	600	1.0	1.14	2.4	

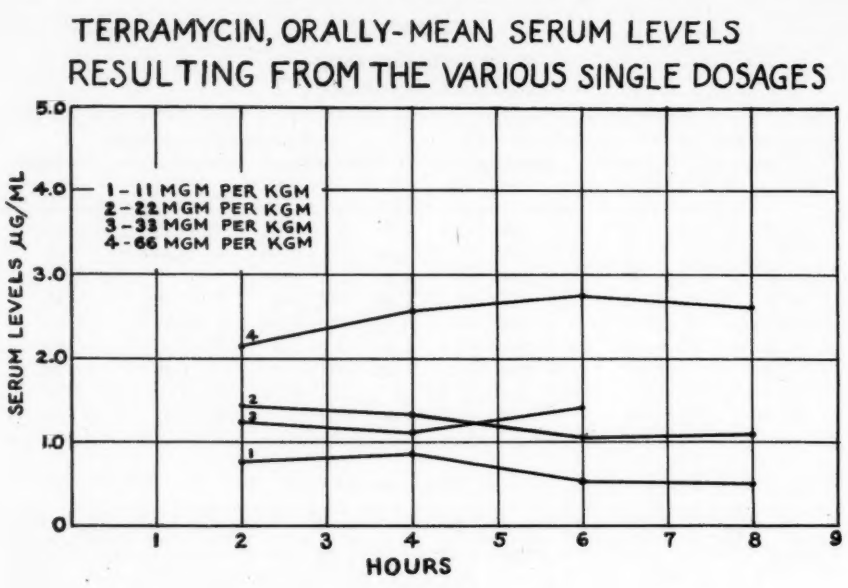

CHART 1

µg./cc. The 4 and 6 hour levels are comparable. The data seem to indicate that increasing the dosage from 22 to 33 mg./kg. had little, if any, effect in increasing serum concentrations (table 3).

With 66 mg./kg., as shown in table 4, there is a tendency for higher serum levels to be attained. Two hour levels range from 0.3 to 4.6 µg./cc., with a mean of 2.16 µg./cc. Four hour levels ranged from 0.8 to 5.0 µg./cc. with a mean of 2.57 µg./cc. Six hour levels were slightly higher, varying from 1.2 to 5.0 µg./cc., with a mean of 2.75 µg./cc.

A summation of the mean serum levels on the four single doses is shown graphically in chart 1.

Intravenous Administration: Terramycin was given intravenously to five patients in dosage of 6.6 mg./kg., and the resulting serum levels are shown in table 5. Values taken at one-half hour varied from 10.0 to 12.8 µg./cc., with a mean of 10.6 µg./cc. The fall in serum level follows virtually a straight line, as seen in chart 2, with mean levels of 2.9 µg./cc. and 1.17 µg./cc. being present at 6 and 12 hours, respectively.

Rectal Administration: Terramycin, 66 mg./kg., was given rectally to four children, with the results being recorded in table 6. Administration was accomplished by inserting perforated capsules with a gloved finger. Retention was satisfactory and little or no discomfort was experienced. In 3 of the 4 instances, absorption is demonstrated, but in one case detectable serum levels were not obtained.

Cumulation: In an effort to ascertain the presence or absence of cumulation, a group of children was given terramycin by mouth every six hours for three days. Individual doses of 11 mg./kg. and 33 mg./kg. were utilized. With the smaller dose no cumulative effect was observed, as shown in table 7. With the dose of 33 mg./kg., however, a definite tendency toward cumulation is observed, as demonstrated in table 8 and chart 3. The

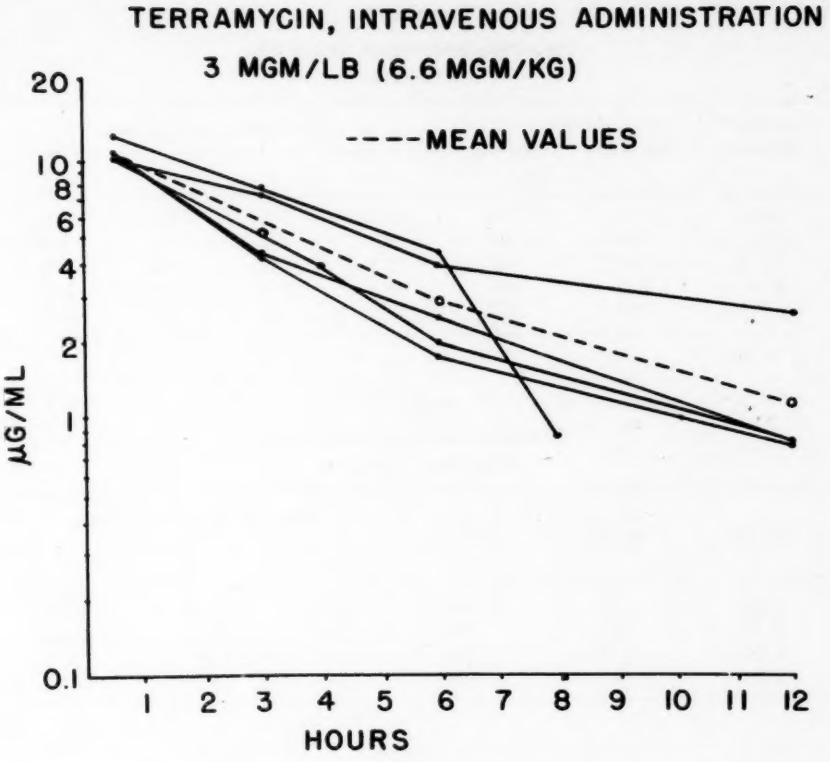

CHART 2

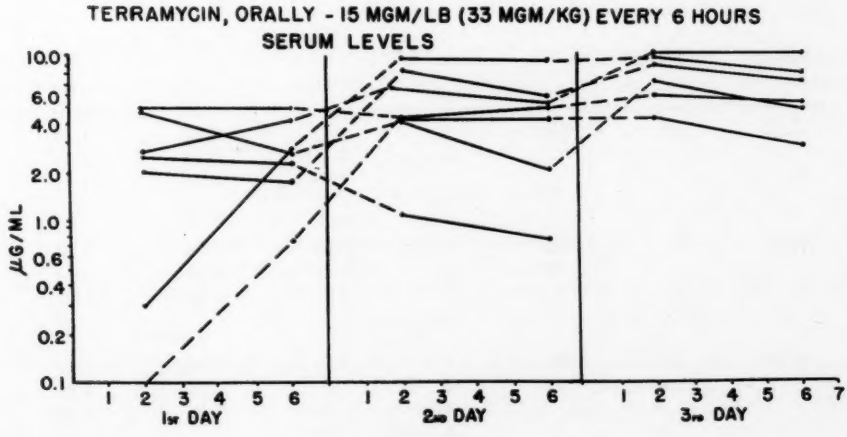

CHART 3

TABLE 5

TERRAMYCIN INTRAVENOUS, SINGLE DOSE

6.6 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Levels, μg./cc. at hours			
			½	3	6	12
J. M.	14	93	10.0	7.6	4.0	2.6
J. W.	10.4	69	10.1	4.2	1.8	0.78
J. J.	13.7	90	12.8	8.0	4.4	0.86
M. B.	19.6	130	10.1	4.0	2.0	0.80
L. F.	30.3	200	10.2	4.4	2.6	0.80

TABLE 6

TERRAMYCIN RECTAL ADMINISTRATION

Single Dose—66 mg./kg.

Patient	Wt. (kg.)	Dose (mg.)	Serum Level, μg./cc. at hours		
			2	4	6
J. M.	14	1000	0.92	0.42	0.33
R. M.	18.6	1250	0.6	0.45	0.32
L. S.	15	1000	0	0	0
J. J.	13.7	1000	1.0	0.35	0.13

TABLE 7

TERRAMYCIN ORAL ADMINISTRATION

11 mg./kg. Every 6 Hours

Patient	Wt. (kg.)	Dose (mg.)	Day	Serum Level, μg./cc. at hours		
				2	4	6
C. J.	48	500	1	1.9	2.15	2.06
			2	2.3	2.55	2.55
			3	2.09	1.46	1.71
			4	1.59		
A. J.	44	500	1	0.86	0.34	0.24
			2	0.88	1.34	0.83
			3	0.97	1.34	1.03
			4	1.1		
S. H.	33	400	1	1.73	2.06	2.23
			2	2.2	2.55	1.87
			3	2.05	1.79	1.46
			4	1.59		

TABLE 8

TERRAMYCIN ORAL ADMINISTRATION

33 mg./kg. Every 6 Hours

Patient	Wt. (kg.)	Dose (mg.)	Day	Serum Level, μg./cc. at hours	
				2	6
J. D.	20	665	1	2.7	4.05
			2	6.9	5.35
			3	10.15	10.6
S. H.	34	1125	1	4.85	4.85
			2	4.4	4.85
			3	6.0	5.68
A. J.	45	1500	1	Too low to read	0.72
			2	4.63	4.63
			3	4.63	3.0
C. McC.	17	625	1	4.63	2.4
			2	4.43	2.05
			3	8.15	5.1
R. K.	25	800	1	2.7	2.4
			2	1.1	0.76
E. P.	30	1000	1	0.3	2.8
			2	10.0	10.0
			3	10.0	8.6
B. R.	10	350	1	2.0	1.76
			2	8.6	6.0
			3	9.2	7.4

mean six hour serum level on the first day is 2.7 μg./cc., while on the third day, it is 8.0 μg./cc.

Diffusion into Cerebrospinal Fluid: In three cases, all free of meningitis or meningeal irritation, simultaneous serum and spinal fluid terramycin levels were taken after three days' therapy, in dosage of 33 mg./kg. every six hours. The results are shown in table 9.

TABLE 9

TERRAMYCIN ORAL ADMINISTRATION

33 mg./kg. Every 6 Hours

Serum and Spinal Fluid Levels After 3 Day's Therapy

(Levels Drawn 5 Hours After Dose)

Patient	Serum Level μg./cc.	C.S.F. Level μg./cc.
1	1.5	Less than 0.4
2	2.4	0.4
3	4.5	0.56

In these cases, diffusion into the cerebrospinal fluid is poor, the CSF level ranging from less than 1/4 to 1/8 the simultaneously obtained serum level.

Discussion

Previous communications from this laboratory[9, 10] have described the difference in absorption between aureomycin and chloramphenicol. Aureomycin tends to be absorbed slowly, probably over several hours, with peak levels being attained approximately four hours after ingestion. Doubling the oral dose from 11 to 22 mg./kg. does not significantly increase the peak serum level. Chloramphenicol, however, is more rapidly absorbed with peak levels tending to be reached two hours after ingestion. Absorption is more complete than is that of aureomycin, serum levels reaching a high order of magnitude and increasing proportionately with the dosage.

The absorption of terramycin is in general similar to that of aureomycin, the almost constant, low serum levels for a period of several hours depicted in figure 1 resembling strikingly the curve for aureomycin. Likewise, increasing the dosage from 11 mg./kg. to 22 mg./kg. and to 33 mg./kg. results in insignificant changes in serum levels. However, a single dose of 66 mg./kg. does cause significant elevation of the serum levels. Such massive dosage was not undertaken in the earlier work with aureomycin.

Of interest is the cumulative effect tending to be present when 33 mg./kg. is given orally every six hours, the effect being present and apparently complete on the second day of such dosage. There is no demonstrable cumulation on 11 mg./kg. This difference is present despite the negligible increase in serum levels resulting from raising the single dose from 11 to 33 mg./kg. A ready explanation for this phenomenon is not apparent.

Such cumulative effect would be of clinical importance if increased antibacterial efficacy could be demonstrated to result from increased terramycin concentration. A suggestion that such might in some instances be the case stems from the work of Hobby et al.[2] These workers, by in vitro studies, showed that terramycin, with a strain of hemolytic streptococcus, was bacteriostatic in concentration of 0.9 μg./cc. Increasing the terramycin concentration to 1.9 μg./cc. produced a bactericidal effect which was still more marked with a terramycin concentration of 3.7 μg./cc. Serum levels above 3.7 μg./cc. were produced in 6 of the 7 patients given 33 mg./kg. orally every six hours.

While such high oral dosage is cumbersome and even intolerable in older children, levels in this range are uniformly achieved with terramycin given intravenously in single dosage of 6.6 mg./kg. Clinical experience in this hospital indicates that 6.6 mg./kg. or 11 mg./kg. given intravenously every eight hours is therapeutically effective and well tolerated.

Penetration of the blood spinal fluid barrier in the case of terramycin is poor and the results in the three cases are similar to those of Herrel et al. mentioned earlier. In general, the penetration into spinal fluid is similar to that of aureomycin.

Chloramphenicol, with spinal fluid levels approaching 50% of serum levels,[10] is the most effective of these three antibiotics so far as diffusion into normal cerebrospinal fluid is concerned.

Rectal absorption of terramycin is unpredictable, and from the data presented here, this route of administration does not appear to be dependable.

Summary

The absorption of terramycin from the gastrointestinal tract is rather similar to that of

aureomycin. Peak levels are low, tend to be achieved in 2 to 6 hours after ingestion, and are prolonged for several hours.

Single oral doses of 11 mg./kg. body weight give peak serum levels ranging from 0.20 to 1.95 μg./cc., with a mean of 1.0 μg./cc.

Doubling or tripling this single dose did not produce marked increases in serum levels.

Dosage of 11 mg./kg. orally every six hours (44 mg./kg./24 hours) resulted in peak serum levels on the third day which were essentially identical with those after the initial dose. However, when a dosage of 33 mg./kg. was given orally every six hours (132 mg./kg./24 hours), marked cumulation in the serum was noted. The mean serum level on the first day on this schedule was 2.7 μg./cc., and on the third day, 8.0 μg./cc.

Diffusion into the cerebrospinal fluid in three cases was poor. With spinal fluid and serum levels simultaneously obtained, the spinal fluid levels were ¼, 1/6 and 1/8, respectively, of the serum levels.

Intravenously administered terramycin in dosage of 6.6 mg./kg. gave peak serum levels at one-half hour, ranging from 10.0 to 12.8 μg./cc. Six hours after injection, serum levels ranged from 1.8 to 4.4 μg./cc., and at 12 hours, from 0.78 to 2.6 μg./cc.

Terramycin given rectally in perforated capsules was well tolerated. However, in four patients given 66 mg./kg. by this route, peak serum levels ranged from 0 to 1.0 μg./cc.

Recommended terramycin dosage: (a) Oral: 11 mg./kg./dose every six hours (44 mg./kg./24 hours). Adequate antibacterial serum levels for most susceptible organisms are produced with this dosage.

Increasing the dosage to 33 mg./kg./dose every six hours (132 mg./kg./24 hours) may be done in cases when high serum levels seem indicated. (b) Intravenous: 6.6 to 11 mg./kg./dose every 6 to 8 hours.

ACKNOWLEDGMENT

The terramycin used in this study was kindly furnished by the Charles Pfizer Company, Brooklyn, N.Y.

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SPANISH ABSTRACT

Estudios de Absorcion y Distribucion de la Terramicina en Niños

Aunque existen varios reportes que estudian los niveles serológicos de la terramicina en individuos adultos ninguna investigación de esta naturaleza se ha hecho en niños y el objeto de este trabajo es el de reportar los niveles obtenidos en el suero con distintas rutinas y dosis de terramicina determinando así su dosificación por kilogramo de peso corporal y en esta forma dar las bases para un régimen racional de la administración en dicho antibiótico en la práctica pediátrica.

Para dicho objeto se cuantificaron los niveles de terramicina en el suero sanguíneo y en el líquido cefalorraquídeo en niños convalescientes y libres de enfermedad renal o cardiaca administrándose dicho antibiótico cuando menos dos horas después del alimento, bajo la forma de cápsulas o de polvo mezclado con jarabe de maíz o bien por vía intravenosa o rectal, Los resultados obtenidos fueron los siguientes:

1°.—La absorción de la terramicina a traves del aparato gastrointestinal es bastante similar a la de la aureomicina; los niveles máximos son bajos, tienden a alcanzar dicho máximo entre 2 y 6 horas después de su ingestion y se prolongan por varias horas.

2°.—Una sola dosis de 11 mlgs./kg. de peso dió niveles séricos que oscilaron entre 0.20 a 1.95 microgramos por c.c. con un promedio de un microgramo por c.c.

3°.—Cuando se dobló o triplicó esta dosis única no se obtuvo un aumento notable del nivel de la droga en el suero.

4°.—Cuando se administraron dosis de 11 mlgs/kg. por vía oral cada 6 horas (44 mlgs/kg. 24 horas) los niveles encontrados al tercer día de administración eran practicamente idénticos a los obtenidos con la dosis inicial. Sin embargo, cuando se dió una dosis de 33 mg./kg. por vía oral cada seis horas (132 mg./kg/24 hs.), se encontró un efecto acumulativo en el suero, pues habiendo sido el promedio del nivel sérico del primer día de 2.7 microgramos/c.c. en el tercer día subió hasta 8.0 microgramos/c.c.

5°.—La difusión en el líquido cerebroespinal fué pobre en los tres casos que se determinó. Cuando ésta se hizo simultáneamente con la de los niveles séricos los niveles obtenidos en el líquido espinal correspondieron a 1/4, 1/6, y 1/8 de los niveles séricos respectivos.

6°.—La administración intravenosa de terramicina a la dosis de 6.6 mlgs/kg. dió una aguja a la media hora que osciló entre 10.0 a 12.8 c.c. Seis horas después de la inyección los niveles séricos oscilaron entre 1.8 a 4.4 microgramos/c.c. y a las doce horas de 0.78 a 2.6 microgramos/c.c.

7°.—La terramicina administrada rectalmente en cápsulas perforadas fué bien tolerada, sin embargo, en cuatro enfermos que se les dieron 66 mlgs./kg. los niveles en aguja del suero oscilaron entre 0. y 1.0 microgramos/c.c.

El efecto acumulativo que se demostró cuando se administró la terramicina vía oral durante tres dias a la dosis de 33 miligramos/kg. tienen una importancia clínica decisiva si se intensifica el efecto antibacteriano, como resultado del aumento de la concentración sanguínea del antibiótico. Tal sugiere la observación hecha por algunos autores en estudios "in vitro" en los que la terramicina actuó como bacteriostática a la concentración de 0.9 microgramos/c.c. contra una cepa de estreptococo hemolítico y como bactericida cuando se elevó la concentración a 1.9 microgramos/c.c., efecto bactericida que fué aún más marcado en una concentración de 3.7 microgramos/c.c. En este estudio se tuvieron niveles de 3.7 microgramos/c.c. en 6 de los 7 pacientes a los cuales se les administraron 33 mlgs/kg. por vía oral cada 6 horas. Es cierto que esta dosis oral tan alta es molesta y aun intolerable en niños mayores, pero cuando la terramicina se administra intravenosamente endosis única de 6.6 mlgs./kg. se alcanzan niveles de dicha proporción y la experiencia clínica nos ha demonstrado que 6.6 mlgs./kg. u 11 mlgs./kg. dados por vía venosa cada 8 horas son efectivos terapeúticamente y bien tolerados. La penetración de la terramicina en el líquido espinal es similar a la de la aureomicina, por el contrario, el cloranfenicol dá cifras correspondientes a un 50% del nivel sanguíneo y a este respecto es el mas efectivo de los tres antibióticos. Los autores concluyen recomendando la siguiente dosificación para la terramicina: a)—vía oral: 11 mlgs./kg. cada 6 horas (44 miligramos/kg. de peso por 24 horas). Con esta dosis se obtienen niveles séricos antibacterianos adecuados para la mayor parte de los organismos susceptibles. Parece estar indicado aumentar la dosificación a 33 microgramos/kg. cada 6 horas (132 microgramos/kg./24 horas) cuando haya necesidad de obtener niveles serológicos altos. b).—Vía intravenosa: 6.6 a 11 mlgs./kg. cada 6 a 8 horas.

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AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

Panel Discussion

THE ACADEMY LOOKS AT PEDIATRIC EDUCATION

LEE FORREST HILL, M.D., *Chairman,* Des Moines, Iowa; GERALD M. CLINE, M.D., Bloomington, Ill.; MILTON J. E. SENN, M.D., New Haven, Conn.; S. RAMCHARAN, M.D., Toronto; CHARLES F. MCKHANN, Cleveland; A. ASHLEY WEECH, M.D., Cincinnati; JOHN MCK. MITCHELL, Philadelphia; HERBERT E. COE, M.D., Seattle.

Chairman Hill: In 1944, the Academy inaugurated a Study of medical services available to the children of America. Included in the Study was a detailed survey of the Pediatric Departments of the 70 medical schools in the U.S. Out of this Study, requiring some 4 years and costing over a million dollars, a vast amount of important information was assembled. As might be expected, the Study clearly showed the enormous advantages possessed by the majority of American children in quantity and quality of medical care, but it also revealed gaps and deficiencies not only in medical care in the field but in the teaching of pediatrics in the medical schools.

In undertaking its Study the Academy assumed a position of leadership among organizations interested in the health and welfare of children. This phase of the Academy's work is now in progress, and while not as spectacular as the Study, it nevertheless is proceeding along a number of fronts on a sound basis. In 1950 and 1951, day-long conferences were held in 9 areas in the U. S. in which pediatric educators, state and regional chairmen participated. This year for the first time in history, the heads of pediatric departments of the Canadian medical schools met under the sponsorship of the Academy's Committee on Medical Education for a 2 day conference.

It seems fitting, therefore, that a place should be made on the program of the Academy's national meeting for consideration by the entire membership of some of the more pressing problems which come under the heading of pediatric education used in a broad sense. The Academy has the unique distinction among pediatric organizations of being able to offer a forum where practicing physicans, teachers and researchists can come together to express their views about common problems in which all have a vital interest. Certainly each group has much to contribute. No discussion of this type has ever before been tried out on an Academy program. Whether it succeeds or fails will depend to a large extent upon the interest shown by the Academy membership.

It was with these thoughts in mind that the panel discussion on pediatric education was arranged. On a Panel is a practicing pediatrician, a professor of pediatrics, a dean of a medical school, a recent medical school graduate, the President of the American Board of Pediatrics, a pediatric surgeon, and a pediatrician with psychiatric training. In addition to the members of the Panel, it is hoped that there will be a lively participation by members on the floor.

Presented at the Annual Meeting of the American Academy of Pediatrics, Toronto, Oct. 23, 1951.

Recognizing that pediatric practice has undergone a definite change in recent years, the main thesis of the panel discussion is as follows: Is pediatric education properly designed to meet the needs of the general practitioner, the pediatrician, or other specialists, public health and the community; at the level of (1) the undergraduate medical school, (2) the internship and residency, (3) the graduate school and (4) postgraduate training?

Dr. Gerald Cline, a successful practicing pediatrician of many years' experience, will open the discussion by giving his views on some of the deficiencies in present-day training for private practice. Dr. Ashley Weech, Professor and Head of the Department of Pediatrics, at the University of Cincinnati Medical School, will discuss the problems faced by the medical schools in their attempt to give all medical students a basic training in practice. Dr. John McK. Mitchell, Dean of the University of Pennsylvania Medical School, who personally made the Academy's survey of the Pediatric Departments of 70 medical schools, will discuss the problem from the angle of the medical school, the internship and the pediatric residency. Dr. S. Ramcharan, a graduate of the University of Toronto Medical School in 1951, will relate to the membership her impression of her undergraduate training in pediatrics as compared to her training in other major departments. Many of us may be in for a bit of a surprise when we think of the training we had compared with that now being given in a top medical school.

One of the important changes in pediatric practice is the increasing responsibility that the pediatrician is expected to assume in parental guidance in emotional growth and development of children. How much of a psychiatrist must the pediatrician become to fulfill this role adequately and how can such psychiatric training be best provided? This question will be handled by Dr. Milton Senn, Professor and Head of the Department of Pediatrics at Yale University Medical School. Similarly, Dr. Herbert Coe, Pediatric Surgeon at the University of Washington Medical School, will point out the great advances which have been made in pediatric surgery and the importance of the pediatrician's being thoroughly familiar with the problems involved.

Finally, the status of the American Board of Pediatrics in the field of pediatric education will be explained by Dr. Charles McKhann, President of the Board.

Dr. Cline: It is an honor to speak as a practicing pediatrician on this panel with so many distinguished teachers and educators of the United States and Canada. Obviously, I cannot speak for the practicing pediatricians as a group, since the practice of medicine is, of necessity, an adaptation of the individual skills and art to a specific situation. Therefore, my comments and ideas on "The Academy Looks at Pediatric Education" are based upon and limited by my own personal experience in a specialty of which I am very proud; and everything I say must be evaluated against my particular background. If I should be wrong in any of my views, I ask your indulgence on the basis of my sincerity and consecration to service in the practice of medicine.

I cannot speak for the Academy nor was I asked to. My assignment is to be the lead-off speaker in this panel discussion, which I was asked to start as a practicing pediatrician who feels that today's formal training does not prepare the young men for some of the particular problems in which I am interested and which have confronted me in my practice.

Thirty years ago today I opened my office in Bloomington, Ill., which was then a city of 25,000 people, for the practice of medicine limited to "Infant Feeding and Diseases of Children." At that time I was an oddity in medicine for there were only 2 other men in Illinois outside of Chicago who limited their work to pediatrics; and in Chicago there were just a few physicians and educators who limited their practice. Needless to say, and with due respect to my teachers, I was wholly unprepared in comparison to the trained board-eligible young men of today. With this brief sketch of my 30 years in pediatric practice, I would like to have you consider certain ideas which I hope may have some merit in planning for sound pediatric education.

Basically, I have 3 major proposals for consideration in planning pediatric education. First, the method of selecting medical students should be changed in an attempt to provide at least a partial solution for the problem of distributing adequate medical care to the entire population. Second, the pediatric educational program should enlist the aid of the part-time practitioner. Third, a preceptorship program should be a part of the training for the future pediatrician.

If we are to provide adequate medical care in all geographic areas, then the choice of medical students is an important problem. The medical institutions that are specifically charged with providing adequate medical service at a state level are the State Medical Schools. Unfortunately, however, these institutions are not inclined to appraise the qualifications of the entering medical student from the standpoint of the distribution of medical care outside of their own states. But

since these State Medical Schools usually must follow a fixed policy, no charge of political interference or discrimination can be leveled against them. Thus we find the private medical schools placed in the anomalous position of having to assume the responsibility for a better geographic distribution of medical care. Perhaps the members of the panel will discuss this point.

I realize that attempts to remedy this situation have been made in some states. Generally speaking, however, these have been exploratory in nature and have not provided any practical solution to the problem. I have been told that one State Medical Society, which set up a fund to pay for educating worthy students who would practice in rural communities for 5 years after graduation, converted its plan into a straight loan fund since 4 of the first 5 students changed their minds and are repaying their loans out of salaried jobs. So the selection of students on the basis of their professed desires which, of course, may change, may not be the answer. Instead, the answer may lie in the strengthening of the educational opportunities of medical students so that their professional growth may continue when they leave the teaching centers.

As concerns the educational program, it seems to me that the young men who are entering our profession are not being adequately prepared for what I see in the practice of medicine today. They are poorly oriented as concerns the social and economic aspects of a medical practice and some of the arts of medicine that deal with translating scientific information into sound pediatric care. In my opinion, these practical problems should be anticipated both at the undergraduate and postgraduate levels.

Let me also call your attention to the marked changes in the type of cases confronting the practicing pediatrician of today which, to my mind, must be anticipated in the educational program of the pediatrician. Years ago I was mainly concerned with infant feeding, communicable diseases, pneumonias and kidney diseases. Today, however, a recent analysis shows that my practice involves in addition to the above: (1) psychologic and psychiatric problems of the child and the home; (2) allergy with its related diseases; (3) severe electrolyte and water balance disturbances which complicate many acute and subacute conditions; and (4) new bacteriologic problems of the old, ever-present acute and chronic infections.

The growth of psychiatry is a necessary product of the times; and it seems to me that psychiatry could benefit from the experiences of the practitioner. The pediatrician is in a unique position to be helpful to the student by his observations, which are experienced in the home, the office and the hospital, thus providing a better understanding of the total family relationships.

Although allergy is still in its infancy, particularly in pediatric medicine, it is very important, as an appraisal of your daily ledger should show. Where should this subject be listed in pediatric education? Again, the man in the field is greatly needed for at least a part of this teaching which has failed to relate the specific allergy problem to the total health of the child.

At what level in pediatric training the subjects of water balance and bacteriology should be stressed is a problem which can best be solved by pediatric educators, for it can be pointed out that these men of today are much better qualified in basic and scientific medicine, which have been so responsible for the most rapid strides in the history of medical science. Certainly we should all appreciate their magnificent contributions. These are the people we must continue to want for our teachers of tomorrow.

In a general pediatric practice a physician cannot afford the luxury of being an expert on emotional problems, allergy, water balance and bacteriology as individual specialists. Instead, he must be well-informed on the practical implications of all the problems of children. Furthermore, I realize that everything a physician needs cannot be taught in his training period, but I do believe that the motivation for the subjects I have discussed should be provided early and should be perpetuated during the training period, not by lip service but by practical exposure to the situations which the physician will ultimately have to deal with when he goes into practice.

The science of medicine and the practice of medicine must go hand in hand with each other, and to accomplish this I recommend that 3 steps be taken. First, I suggest that the entrance examining board of every medical school should have at least one member who is a part-time practitioner. I believe such a man would make a significant contribution to the evaluation of aptitude testing, grades, background history of the applicant and perhaps the geographic distribution of the future doctors who may be pediatricians. Second, I suggest that there be a sufficient number of part-time pediatric practitioners on the rosters of our medical school faculties. In connection with this, I suggest that even greater emphasis must be placed upon having a teaching staff (part-time or full-time) that is interested in the broad aspects of the sick and the well child and will teach this information meaningfully to the students. The selection of teachers is of equal or even greater im-

portance than the selection of students. Third, I strongly advocate a preceptorship program which is so individualized that it will be adaptable to the variations of the locality and the community in which the pediatrician will serve.

Medicine is, in part, being socialized by the profession itself because graduates are finishing their internships and residencies with too much concern for finding salaried jobs, which require only a 5 day week and an 8 hour day. Often this same group (both men and women) were the early candidates who, with high scholastic grades and ratings, were given a preference for entrance into medical school over the hard-working young man, ready to devote his life to serving the public and his profession. Undoubtedly many such men and women of this type are being eliminated from the study of medicine by the increasing cost of a medical education.

Where is the young pediatrician to learn and how does he learn the art of practice? Does the young doctor himself know the methods of satisfying the parents, grandparents and referring doctors? Where does he learn office technic? Is he impressed with his civic responsibilities? By consecrating himself to service for his community as a whole, he will attain a degree of pride which pays largely in dividends of self esteem.

What about the business side of a practice? Undoubtedly the signs of the times with inflation make it impossible for the young man of today to know the value of a practice. There are far too many looking for what they can get and thinking but little about what they owe and can give to their patients and to the professional ideals of the past. This is not unique to medicine; it seems to permeate all of our culture today. No doubt we men in the field can take some of the blame for this by our example of standards of living and practice. How can we, however, prove to them that we did not live by the same standard in the beginning; that by consecration to service, investing in our own business, leadership in our communities, even with lesser professional competency in those days, we have attained our status of today? This takes time. To have become good pediatricians we have had to let the practice of medicine be our yesterday, our today and our tomorrow.

Up to this point I have not discussed preceptorship which, in my opinion, actually carries the major answer we have today for these various problems of educating the future practicing pediatrician. It is as old in many ways as medicine itself, yet apparently very new in pediatric education. As you know, it is also a much debated subject among educators and has not been accepted generally as part of the course of postgraduate education in pediatrics.

For almost 15 years I have had a residency program under the guidance of our State University whereby the postgraduate student spends 6 months of his 2 year program in Bloomington away from the parent-teaching institution in Chicago.

During this time I have had quite a number of young men and women with me who have had various personal ideas, criticisms and commendations for this type of postgraduate education. Primarily, the Art of the Practice and the business side of medicine have been the main objectives.

The daily tasks of my residents are numerous and complicated. Institutional care of a state school for children with a population of 325, hospital rounds on an active private pediatric service, journal clubs, local staff and county medical society meetings, and the teaching of pediatrics to student nurses are part of their duties and training. The important part of the entire program, however, is the time spent in my office with private patients when they learn and see what type of cases an active practice is composed of. Here they learn the art of handling the child and how to satisfy the parents, the grandparents, and the referring doctors; plus the business side of medicine, including the technic of keeping records, making charges, bookkeeping and insurance. At the Illinois Soldiers' and Sailors' Children's School, where they work and live, they are fortunate to have the consultation staff of the Institute for Juvenile Research in Chicago spend 2 days a month at the X school, where their exposure to psychiatric problems is extremely large and valuable.

They travel with me on house calls and out-of-town consultations. They are given a course, so to speak, in budgeting time and money in an office and home, where they are shown actual social and economic problems as they exist in their natural setting. They not only go along to PTA meetings but are used as guest speakers for such organizations. They assist in our polio center of active cases and also the monthly clinics for crippled children. They are also responsible for the medical service in the McLean county summer camps for crippled children.

The entire preceptorship picture, to my mind, is of great importance in this 2 year residency program. It is debatable whether this 6 months' period should come early in the 2 year residency program. Personally, as I see it now after having had at least 12 or 15 students go through this

service, I feel that the last 6 months of this 2 year training should be devoted to the preceptorship period. In other words, at this particular time they have seen it all and are now older, more stable and ready to see and comprehend what lies before them as they enter private practice. Also, the student who is interested in teaching will benefit by having had this exposure and experience in private practice.

My personal experience leads me to believe that the preceptorship program is something the young men need and appreciate now perhaps as much as any part of their residency; and in the years to come they will realize more than ever the truth of this statement. However, it will take them several years to acquire a full appreciation of the value of the preceptorship program.

In conclusion I want to re-emphasize these points: 1. There should be a more discriminating selection of medical students. 2. The pediatric educational program should enlist the aid of the part-time practitioner. 3. The preceptorship program should be an important part of the training of the future pediatrician.

In preparing this paper I realized that the subject matter and my approach to it would be open to criticism in many of its phases. However, if I have presented material which will lead to constructive discussion, I feel that the underlying objective has been accomplished.

Dr. Senn: Pediatricians and general practitioner caring for children must have:

1. Knowledge of the processes of personality growth and development with understanding of the factors which determine behavior.

2. Knowledge of the dynamic qualities in parent-child relations and of their role in molding the personality and character of each human being.

3. Knowledge of the role of the physician and the persons associated with him (hospital personnel, etc.) in influencing behavior of children and in modifying attitudes of parents.

4. Understanding of the more effective use of interviewing (history taking) and of the physical examination in helping people psychologically.

5. Greater awareness of the community resources (child guidance clinics, schools, recreation, etc.) and their values when included in comprehensive pediatric planning for a child whether he be well or sick.

Pediatricians in training should have opportunities for observing, listening to, and talking with children of all ages, well and sick, in different settings (well baby clinics, nursery schools, elementary schools, hospitals) where the same children may be observed over a period of time (the longer the better), instead of cross sectionally, where the trainee is provided with a teacher who, by experience and knowledge, can help the student to observe, record, contemplate and understand what is noted. Provision should be made for pediatricians in training to have contact with teachers of different disciplines, both within and outside of medicine, who can translate and apply knowledge about growth and development within the framework of pediatric care so that the trainee becomes aware of his opportunities as well as his limitations in dealing with the psychologic aspects of child care, and being always alert to the emotional implications of everything a physician says and does. Teaching of medical psychology must not be isolated from teaching the child in all other respects.

Dr. McKhann: There are other purposes of pediatric education than preparing the student to pass Board examinations. Specialty boards have been the subject of controversy not because of the action of the Board, but because of uses that have been made on Board certification.

The American Board of Pediatrics is composed of 9 members, 3 representing the American Academy of Pediatrics, 3 the Pediatric section of the American Medical Association, and 3 the American Pediatric Society. The function of the American Board of Pediatrics is to establish standards of proficiency for the practice of this specialty, to determine the training and experience required of each candidate, and to examine and certify candidates who meet the standards of education, training and experience, and who pass the examination. The American Board of Pediatrics has representatives on the Advisory Board of Medical Specialties, which meets periodically to discuss the problems common to all the Specialty Boards. It is the privilege of the American Board of Pediatrics to establish Sub-Specialty Boards as it so desires. For example, there is now a Sub-Specialty Board of Allergy under the Board of Pediatrics. It is possible that in the future other Sub-Specialty Boards may be set up.

The American Board of Pediatrics actually has no other function. However, because it sets the standards which must be met by persons seeking certification as specialists in pediatrics, it becomes

interested in the education and training of the candidate, both undergraduate and graduate. The American Board of Pediatrics exercises no jurisdiction in any way over undergraduate pediatric training, but does have a considerable influence in postgraduate training in that it advises the Council on Medical Education and Hospitals of the American Medical Association regarding approval of residencies. It is to be noted that the American Board of Pediatrics does not approve or disapprove residencies, but does give its best judgment to the AMA Council on Medical Education and Hospitals as to those residencies that should be approved. While this is an ancillary function of the Board, it is deemed an important one in order to protect the resident in training from inferior types of training which he might unwittingly take and which would ill prepare him for the examination. Hence, it would seem that, while the American Board of Pediatrics has no direct influence on medical education, it does in actuality have a very considerable influence. For this reason the constitution of the Board becomes important.

The majority of the men on the Board are in practice, the minority are professors. Each section of the country is represented. In addition to the members of the Board, the Board as a group selects from various parts of the country men to assist and aid in the examinations. They are designated official examiners. It is not intended that the examinations of the Board should set standards attainable only by full time instructional staffs in medical schools, but should set standards for the man in practice or who intends to be in practice, and standards of a minimum rather than of a maximum height.

Dr. Ramcharan: I have been given the great privilege of speaking on behalf of all medical students before this distinguished gathering. My discussion concerns undergraduate pediatric training, and my comments are based in part on opinions of students in the United States and Canada.

In general I found the study of children in their normal and abnormal states a fascinating one. Learning how to get along with your little patients, how to interpret their every cry, how to induce them to cooperate on a physical examination, for example, how to persuade them to put out their tongue when they state a blank "no" to your request to do so, all this, I say, can be a very interesting experience.

I have been asked whether I felt my undergraduate training left me feeling adequate to undertake the care of children as a hospital interne or in general practice. To this question I would answer no. This is so because I did not receive adequate training in clinical problems. This is especially true of the common diseases of children and communicable diseases, all of which are of particular interest to the general practitioner. In addition some clinicians tend to show rare cases and diseases rather than ordinary illnesses. This lack can be made up for by starting clinics in pediatric medicine during the third medical year and spending more time in the outpatient department, for it is only by experience with clinical problems that the theoretic knowledge acquired from lectures can be given practical application. We should also be given more cases to work up on our own. Especially did I feel the lack of clinical experience in the communicable diseases. For the diagnosis and handling of these form a common practical problem in general practice. Another way in which clinical experience could be achieved is by a period of living-in in hospital as an undergraduate. We appreciate the difficulties involved in such an arrangement but it is something that we can look forward to. Of course it must be understood that facilities differ in the various schools and what is true of some is not true of others.

I also feel the need for practical knowledge of the normal and abnormal growth and development of children. Lectures may be valuable and can be made as practical as possible by the liberal use of slide demonstrations. However, after a time it becomes difficult to absorb what is largely theoretic knowledge. I think that more time spent at well baby clinics would help to solve this problem. There we should be given the responsibility for the treatment of children, advice to mothers regarding changing of diets and other such problems. In this way we should become familiar with the normal child and the variations from the normal. The difficulties inherent in such a program are only too obvious. Busy practitioners who run the clinics can ill afford to give the time required by inexperienced students.

I feel inadequate to meet the problems in adjustment that arise in child development. We received well organized lectures with descriptions of the possible abnormal forms of neurologic and mental development in children, but did not acquire a proper perspective of the field nor did we have the opportunity to observe the method of handling common behaviour problems.

As far as lectures are concerned the usual criticism may be made that too much time is spent

copying out notes at lectures, which time could be more profitably spent for practical demonstrations. We are not unmindful of the value of lectures but feel that more use could be made of mimeographed lecture notes thus saving time for discussion. Secondly, we often observe that a clinical teacher is unprepared when he appears before a class. Thirdly, instructors sometimes fail to appear for a scheduled class without notifying the students. However, the reverse is also true, and I have known of instances where the students have called off classes and have not notified their own clinician. Lastly, since clinicians in large hospitals are specialists we thought that it would prevent an undue stress on one aspect of children's diseases if clinicians rotated among the groups of students receiving instruction.

Some students mentioned that they would appreciate hearing some of the common ordinary business of starting practice and looking after pediatric patients.

Comparing our training in pediatrics with that obtained in medicine and surgery, the chief difference is that we had no opportunity for undertaking the responsibility for the care of children such as we had in the outpatient department in our course in medicine, or in the clinics or emergency department in our course in surgery. Of course, we understand that this opportunity depends on the facilities available. However, it becomes a serious drawback for one considering general practice, especially when there is no opportunity for experience as a junior interne on a pediatric service.

As far as comparison with obstetrics is concerned the opportunity for living-in hospital is a definite advantage on the side of obstetrics. Also it may look well on paper to have a combined obstetrics and pediatric term. In practice we found that this did not allow for intensive study of either subject. Because of this I think that one half of the term should be allotted to obstetrics and half to pediatrics.

On the whole we enjoyed pediatrics and I think that we had an excellent course. Our teachers were always patient and helpful and I think it would interest them to know that students appreciate it when an instructor criticizes statements made by them or methods of examination and treatment so that they know definitely they are right or wrong. I hope these comments will go some way in helping to further understanding between teachers and students so that teachers will be able to derive pleasure from their work of helping us to acquire an understanding of what at first are to us strange wriggling creatures in other people's arms.

Dr. Weech: Since the primary purpose of our Panel is to bring out into the open existing inadequacies in pediatric education and since this purpose will best be served by discussion and challenge from the floor, my prepared remarks must be brief and, if possible, provocative of discussion. I shall make no attempt to cover all controversial issues concerning adequate undergraduate teaching—issues discussed in more or less detail in the 1949 Report of the American Academy of Pediatrics on *Child Health Services and Pediatric Education*. The exigencies of brevity demand confining myself to selected issues which to me seem important. Perhaps the very act of omitting many other items will provide the stimulus for free discussion.

I shall begin by daring to ask whether we who are doing the teaching are indeed qualified for the job. The trend of organization in departments of pediatrics is in the direction of the full time system. The professor and as many of his associates as the budget will allow have abandoned the type of medical life which most of the students will follow. Often they have been attracted to the academic atmosphere by the opportunity to engage in research rather than by a compelling desire to teach. In stating this fact there is no wish to deny the conviction that a qualified investigator trained to question established beliefs will in the long run be a better teacher than he who, however eloquent, merely reiterates the dogmas of his time. There is also no desire to oppose the assertion that time to devote to teaching and time to prepare for teaching coupled with years of practice in the act of teaching will in the long run produce a better teacher than when the job must be done on a hurried part time basis. Nevertheless it is relevant to point out that the full time teacher and investigator has rarely received instruction in what may be termed "the art of teaching." This circumstance is an item deserving serious thought.

The full time teacher must also guard against another inherent weakness. Most of his students will become practitioners encountering petty and minor problems from which he himself is protected. It is hard to teach effectively what is not a part of experience. In most divisions of pediatrics the full time teacher is flanked and helped by a group of medical practitioners. Beset with the cares of private practice they rarely have time to construct an integrated curriculum. Their aid in the over-all

program is nevertheless indispensable. I salute them for what they have done, for invariably the contribution is voluntary and without compensation. But, likewise, it is true that they too have rarely received training in the art of imparting knowledge.

What then is the goal of teaching? There are 2 essential ingredients, facts and the use of facts. Factual knowledge is gained in many different ways. Books, journals, pictures, didactic classes, conversation with teachers and talk with other students, all have a part to play. The student must also learn to grasp facts from observation. Herein lies a primary reason for teaching at the bedside with small groups of students who are learning by experience how to see, how to hear, how to feel the normal and departures from it. Cultivation of curiosity gives incentive to the art of observing. Well do I remember a fourth-year bedside class with Dr. Edwards A. Park. "Look," said Dr. Park, "the baby's gums are white. Why," and he looked at me, "are the gums white?" I confess I had not noticed that the toothless gums of infancy are often pale in contrast with surrounding mucous membranes. I hazarded a guess that perhaps teeth preparing to erupt had obstructed the circulation. This concept was discussed at length and discarded as being inadequate to explain the distribution of the pallor. My curiosity was climbing. Then, Dr. Park confessed he did not know himself what made the gums white but that someone ought to find out and let the group of us know. One of our greatest teachers had driven home a point. Be constantly curious about the things you see! No detail is too small to merit questioning observation! In this way only will eyes, ears and fingers continue to add facts to your storehouse of knowledge.

The importance of factual knowledge can scarcely be overstressed. No amount of reason can reach a sound conclusion when factual knowledge fails. I remember vividly the plight of a greatly perplexed intern at Monday morning rounds after he had admitted and studied over the weekend a boy with Friedreich's ataxia without making a diagnosis. At the rounds the nature of the illness was recognized at once by a number of his teachers. On the way to lunch after the rounds were over the intern vocalized his perplexity. "What do you do," he said, "when you have taken the most careful history you know how to take; what do you do when your physical examination has been as detailed as you know how to make it; what do you do when neither history nor examination give any clue toward making a diagnosis? I know I should go to the library but how does one proceed to look the subject up when he does not have the foggiest notion of what subject to look up?" A sympathetic feeling bit me to the core. Indeed, does the doctor exist who had not experienced this intern's plight? With measured words I answered, "Some fact from the anamnesis, some fact from observing the patient, must tinkle a bell in the cortex of experience. Pitch and position of the bell are relatively unimportant. The essential thing is that some bell tinkles. And, the more bells that ring, the more clues for library research."

The conclusion is clear. In teaching medical students facts must be imparted. The greater the number of facts, the better prepared is the student for the problems of future practice.

So clear is the conclusion that another danger emerges. The teacher in his enthusiasm to present the latest knowledge, in his meticulous care to cover each minute detail, may find that time is short, and invariably he talks too much. "Spoon feeding," the students call it and the better students know that the method is not good. Facts are to the physician what tools are to the craftsman. They are essential but serve their purpose only when the student learns to use them in sound habits of drawing conclusions. Better fewer facts and more practice in the use of facts! How to mold the minds of men is a challenge to better teaching. After nearly 30 years of pedagogic contact with students in 4 medical schools, I still feel inadequate to meet this challenge as some day it should be met.

When we teach system in taking histories and doing physical examinations we are moving in the right direction. "System," Osler wrote, "is the harness without which only the horses of genius may travel." Yet we do not bring enough system into guiding processes of thought as the student weighs the facts at hand and gropes toward a diagnosis. As one of the oral examiners of the American Board of Pediatrics, I have been distressed over a number of years at the relatively small number of candidates who seem able to systematize their discussion of problems in a way that makes it impossible to forget for the moment significant aspects of the topic. I feel certain that teachers can be taught to encourage orderly habits of thought.

I have experimented with another technic of avoiding "spoon feeding." Perhaps some of you may wish to try it. The situation deals with case presentations before small groups of students where the traditional technic is to have one student, assigned to the case, present the history, physical findings, results of laboratory procedures, etc., and finally his diagnostic impressions. In the experimental tech-

nic the traditional approach is abandoned completely. The student familiar with the details of the case acts the role of the patient's mother. His classmates ply him with questions until a history has been extracted. Then, the student changes his role and acts the part of the patient's family physician who is familiar with the findings on physical examination and in the laboratory and who consults the class for help in making a diagnosis. All the essential information is brought out by active questioning from the class. The teacher merely attempts to guide the direction of questioning when it tends to run off on a tangent.

There is not time this morning to go into more detail. The technic is offered as one which makes it possible to guide the paths of thought of perhaps a dozen students in the class. I may add I am often amazed at the power of collective thinking in bringing to light aspects of a problem which no one student could have coped with alone.

There is still another method of training the mind to use facts soundly. It is a method most often employed at staff ward rounds where interns and residents are the students but it can with profit be extended to undergraduate teaching. I refer to the presence at class case presentations of more than one teacher each of whom has specialized knowledge in a field pertinent to evaluation of the over-all problem of the patient. One teacher, of course, must be master of ceremonies. The student presents the case and so occupies a pivotal point. He must be kept at the pivot by constant reference to him for the facts of the patient's problem. But, the emerging discussion sheds on the issues the light of specialized knowledge. Not only are facts imparted but the facts come out in a situation charged with the need to reason. Error of reasoning meets the challenge of greater acquaintance with fact. This is an atmosphere to incite the mind to grow.

In conclusion, I wish to state again awareness of having touched only the fringes of the problems of undergraduate pediatric education. Some of what I have said is pertinent to teaching in all the professions. Much of it is applicable to the other clinical specialties. Specific items pertaining only to pediatrics have perforce been omitted. I have chosen to discuss the teaching of "facts and the use of facts" both because of basic importance and also because by concerted effort improvement can be wrought.

Dr. Mitchell: I have been presented with a few questions to which I am going to try to give you some very simple answers. Time does not permit me to defend my answers.

The question has been raised as to whether pediatrics is assigned a sufficient number of hours in the curriculum to handle the subject properly.

There is no question but that prior to 1946 a large percentage of people who were concerned with the decision as to how many hours should be devoted to various departments looked upon pediatrics as a specialty that was concerned purely with infant feeding, diarrhea and the infectious diseases of childhood. At that time a large number of pediatric departments in the various medical schools were not assigned a sufficient number of hours to teach the subject satisfactorily. During the intervening period there has been an increasing realization on the part of deans and curriculum committees of the true role of pediatrics, and the situation has changed materially for the better. I hope that the Academy study was of value in this particular regard, and I think it was, because it pointed out clearly that many pediatric departments must have a greater number of hours if they were to fulfill their function properly. Today I feel no concern about whether pediatric departments in general are allotted a sufficient number of hours to carry out their teaching program. Hours are apt to be assigned where they can be best handled. A department of pediatrics is not strong because it has a large number of hours allotted to it; rather, a strong department will have ample hours assigned.

Question: Do pediatric departments have adequate budgets?

Any of you who are really familiar with medical school financing will understand the complications of this problem. A budget committee is not given a certain sum of money and then told that it may distribute this money as it considers best. Instead in a large proportion of schools there are departments that have been existing for many years on a set budget, often derived from endowed funds which must be used for a specified purpose. These departments have a staff of professors, many of them with tenure; you cannot suddenly change this picture. Some pediatric departments have adequate budgets, others are woefully inadequate. It is a complicated and difficult problem which cannot be answered in a single statement or solved by a single decision. Only by making available a considerable sum of money which can be used wherever needed for operating expenses can a start on the solution be made.

Question: How can training at the undergraduate and graduate level be improved, particularly

in view of the finding of the Academy study that 75% of all child care is done by general practitioners?

A figure that has not been used as much as the above but which is actually of greater significance is that between 30 and 35% of the general practitioner's time is spent with children. It seems to me that this points to a matter of great importance, namely, that it is not the duty of pediatric departments to try to make pediatricians of students at the undergraduate, or of house staff at the rotating intern level. Rather it is their duty to train students and interns in such a manner that they will become physicians who understand the problems and the care of children; that they may be in a better position to undertake that care no matter what their type of practice may be. The tendency to train students during undergraduate and intern years as if they were entering that specific specialty is a fault to which all departments are prone.

Another error which has frequently crept into pediatric teaching, at least so I am told by a considerable number of students with whom I have discussed this problem in various schools, is that of teaching on rare cases only. I realize fully the reasoning which lies behind this method of teaching. Its proponents hold that they are not attempting to have the students learn about this particular disease, it is rather a procedure to teach students how to approach the study of a case, a method which will hold for all cases. You cannot always depend on student criticism, yet I agree that is a legitimate criticism if it is applied in the broad sense. One student expressed this well when he said, "If I were on the western plains and saw a large four legged animal at a great distance and some one asked me what that animal was, I could make a pretty good guess, because I have been raised on the western plains and know that the chances are all in favor of its being a cow. But," the student continued, "I am just now going into practice and if you placed me in a similar situation in medicine and asked that question I wouldn't have any idea of the answer." Thus, a "common complaint" among students is lack of familiarity with "common complaints."

Another field in which students find themselves at a loss is in that of growth and development and in the behavior problems of children.

Question: How can internship training be improved?

No one will deny for a moment that the internship should be an educational experience and not a service for the hospital. The chief difficulty with our internships—I am speaking now of rotating internships—is that the amount of time allotted to pediatrics on the rotating internships is far less than it should be. As an illustration, one state board allocated 2 weeks to pediatrics and 8 weeks to laboratory service. Anyone who practices today knows that this is a totally disproportionate allotment of time in terms of the relative importance of these 2 experiences to the practitioner. I am happy to say that in this particular instance the ruling has now been changed, although they are still assigned equal periods of time.

Well baby care is a field in which many rotating interns receive no training. Further, in view of the shift in the type of pediatric practice which has been taking place in recent years, namely, the great increase in ambulant care, our rotating interns do not get enough experience in the outpatient department.

The question has been raised as to whether 2 years of residency training is sufficient to properly prepare pediatricians.

The answer, it seems to me, lies almost entirely in what you are trying to accomplish. If pediatrics is to be a highly specialized subject, if pediatricians are to be, in the main, consultants, as has been largely true in Great Britain in the past, then I would say the answer is "No, two years is not enough." If however, you look on pediatrics as more or less general practice applied to an age group, then it is my opinion, that 2 years is sufficient. Please understand, I do not mean that this amount of training is sufficient for the man who plans to teach, or for the man who hopes to become primarily a consultant, or for the man who is going in some specialized field or into research. The 2 years of residency required by the Board of Pediatrics is regarded as the minimum necessary for the practice of satisfactory pediatrics; others can take more time and a large proportion of them do take more than 2 years of residency training.

Question: What is the role of the graduate school in pediatric training?

Personally I do not feel that the graduate school should be looked upon as a substitute for residency training. It should rather be considered as a supplement to residency training, because by the nature of the system under which graduate education is set up in most graduate schools of medicine, it is not possible to give the students responsibility for the care of patients. If they do

not have this responsibility, then the whole experience is totally different and should not be used to supplant residency training. The graduate school undoubtedly has a real place; it is especially useful for those who have had poor basic training. For a large percentage of foreign students whose basic training has either been different from ours or not as good as ours, the graduate school offers a method that is probably superior to an equal period of time spent in residency training.

Question: Has the plan of rotating residents from teaching services and pediatric centers to outlying hospitals been successful?

Dr. Cline has touched on this problem and his experience is undoubtedly wider than mine. I can say from what little experience we have had with it ourselves, that it is an effective method of widening the experience of the resident, particularly when the rotation is from a highly organized teaching center to the small rural hospital with a good staff. I personally would be inclined to think that the amount of time which Dr. Cline feels should be included in the rotation is too long. If speaking in terms of 2 years of residency training, 6 months seems to me to be much too long to spend on the affiliated service. Our own residents feel that 2 months is ample.

Dr. Coe: One of the main objectives of our Academy is better care for children. Today we are concerned particularly with the place of education in that better care, and it is my assignment to direct our attention to the surgical aspects of that education. Children's surgery has progressed markedly and become increasingly complex from the not too distant past when it was often thought to be concerned mainly with circumcisions and the removal of tonsils and adenoids, to the present time with our intricate procedures which are saving many children who were formerly doomed. We may well ask whether education has kept pace with that progress.

Should better surgical care for children be developed in relation to pediatrics or to surgery? In which department in medical schools should it be developed? What about those practitioners who have passed beyond their undergraduate days? Should the subject be called "surgical pediatrics" or "pediatric surgery"? Would it not be better to correlate it with the child as a whole and speak of the "surgery of and evolutionary period"? Is there any real necessity or demand for improvement in this aspect of better care for children? Such questions are being asked with increasing frequency.

Let us consider the last question. There is very little demand from surgeons, from surgical departments of medical schools, or from surgical organizations, for the development of the subspecialty of children's surgery or for surgical training directed particularly at the requirements of this age period. There is, by contrast, a constantly mounting demand for such training from the practicing pediatrician who is in daily contact with the average children's surgery throughout the country. The demand comes also from the professional and nursing staffs of hospitals and from internes and residents. Internes and residents too frequently have seriously inadequate knowledge of surgical conditions in infants and children, neonatal emergencies, time of election for surgery, preoperative and postoperative care and medication, possibilities and prognosis of surgical treatment, technical problems, the gentle pediatric approach to the patient, the highly important tactful and sympathetic handling of parents. I believe we can say that there is a definite necessity and demand for better education.

Where the subject is placed in the curriculum and what it is called is largely an academic question to be determined locally. There will be found, however, a rather definite resistance on the part of many surgeons to the development of more surgical specialties, the "splitting off of more segments from general surgery," but such narrow personal prejudice should not be permitted to interfere with the development of better surgical care for children.

What about the general surgeon and the general practitioner?

The Academy study of child care indicated that at least 75% of children are cared for by the general practitioner and I believe it is a conservative estimate that 80% of the surgery on infants and children is done by the general surgeon and the general practitioner. What is their training? Largely experience—an excellent school in many respects but a costly one. They are often unfamiliar with the advances of technics which are so rapidly developing; their honest opinions are most diverse; and they are usually even more eager for information and education than are the internes and residents.

With these problems of education in mind, what constructive suggestions can be made?

In my opinion our Academy with its diverse membership including educators, practicing pediatricians, surgeons, and employes of governmental agencies, is in a unique position to initiate

and correlate activities for improving the care of children by improving education. To obtain the best and most immediate results this should be carried on simultaneously at the undergraduate, interne-resident, and postgraduate levels. I realize that for many reasons this will be extremely difficult but the following suggestions are presented for your serious consideration:

At the undergraduate level it is suggested that as a minimum there be specific instruction by qualified persons on (1) the basic principles of the surgery of infancy and childhood, stressing the characteristics of this period, (2) the technical variations from the patterns of adult surgery and (3) the surgery of the congenital defects.

At the interne-resident level the instruction should be not simply in the operating rooms but in all departments of the hospital—clinical laboratory, bedside teaching, outpatient department, etc., and should be directed by those individuals best qualified for that assignment. Such training should be carried on in any hospital approved for interne training but should be required in those approved for surgical residencies.

At the postgraduate level every effort should be made to reach the practicing portion of the profession. Formal postgraduate courses should always include some subject relating to the surgery of infancy and childhood just as definitely and routinely as those relating to the malignancies of the older age groups. Teams should be organized to present the current and newer concepts of children's surgery before county societies reaching those practitioners who are unable to travel to centers of education for refresher courses. As individuals we should publish appropriate articles in the medical literature, and address smaller groups, such as hospital staff meetings and special societies as often as possible.

By way of a summary, may I suggest a definite coordinated course of action which the Academy can perhaps sponsor and which might be called a "seven point program."

1. Through our Committee on Medical Education we should request appropriate training at the undergraduate level.

2. Through our Committee on Medical Education we should develop departments or subdivisions of children's surgery in medical schools. (I am happy to say that in several medical schools this is now being done.)

3. As individual members make it our responsibility to request the development of departments of children's surgery in the larger hospitals in which we work.

4. Suggest and recommend rotating general internships through children's hospitals whenever they are available. I know that internships are crowded, but wherever a children's hospital is available it will be a valuable addition to a general internship.

5. Request the American Board of Surgery to include questions on children's surgery and to notify candidates that such questions may be included. This can be done through our Section on Surgery, as one of our members is on the American Board.

6. Urge the American Board of Surgery to include in its eligibility requirements a period in a children's hospital when such a hospital is available.

7. Request the Joint Commission on Accreditation of Hospitals to note facilities for the surgical care of infants and children.

Discussion

Dr. Edward S. O'Keefe, Lynn, Mass.: I have noted an error in the title of this morning's panel discussion. Instead of the "Academy Looks at Pediatric Education" that title should read "Pediatric Education Looks at the Academy."

Before I go any further I would like to say that I have no prejudice against teachers. My father was a teacher, my brother and one of my sons are teachers; I, too, have been a teacher.

Now what are the functions of a teacher? Obviously 2 of the most important are research and teaching the students.

How well qualified are the present day teachers to perform these functions? We can dismiss the first category with a word "They are well qualified." Let us consider the second category—in the medical field, teaching the students means teaching them to practice medicine. To practice medicine where? In the hospital and/or in private practice? The answer is, they practice in both places. Since the majority of students will ultimately enter private practice this last category is the more important.

Are our present teachers well qualified to teach the students how to conduct their work outside the hospital? Since the majority of full time teachers of today do not and, moreover, have never practiced medicine outside of a hospital I believe the answer is no.

What is the remedy? It seems to me that an important qualification for teaching is at least 3 years' experience in private practice in the specialty in which the man expects to teach. A good way to attain this important goal would be to require such an experience in private practice as one of the qualifications for certification in any of the specialties or in general practice. A man can't very well teach students how to do something which he himself has never done.

The man in private practice must be reinstated in the teaching programme of our schools and teaching hospitals.

Round Table Discussion

PEDIATRIC ALLERGY

C. COLLINS-WILLIAMS, M.D., *Chairman,* Toronto;
BRET RATNER, M.D., New York City

HOWARD J. MORRISON, M.D., Savannah, Ga., and
W. EUGENE KEITER, M.D., Kinston, N.C., *Secretaries*

SPECIFIC DIAGNOSTIC PRACTICE

Chairman Collins-Williams: The specific diagnosis of the child with respiratory allergy comprises the following: (1) general pediatric care; (2) careful allergic history; (3) complete physical examination; (4) indicated laboratory procedures including nasal smears; (5) skin testing.

Skin testing is necessary in order to help determine the specific etiologic allergens. The allergens tested with should include the common foods and the common inhalants, pollens and molds in the environment.

EOSINOPHILES AND EOSINOPHILIA

Eosinophilia occurs in a great many conditions other than allergy and these must be taken into account in interpreting differential blood counts.

The nasal smear is a useful laboratory test in the diagnosis of nasal allergy. Eosinophiles may temporarily appear in considerable numbers in the nasal smear of the nonallergic child during recovery from a respiratory infection, but otherwise a predominance of eosinophiles in the nasal smear is diagnostic of nasal allergy.

OFFICE TREATMENT OF RESPIRATORY ALLERGY

The office treatment of a child with respiratory allergy includes the following: (1) general pediatric care; (2) symptomatic relief of allergic symptoms; (3) removal of incriminated foods from the diet; (4) as complete an elimination of environmental allergens as possible; (5) specific desensitization.

SPECIFIC DESENSITIZATION

Dr. Ratner: The method of specific desensitization which we use in practice is as follows:

The treatment extract consists of a 1:5,000 dilution of each of the inhalants, pollens and molds with which the patient gave a positive reaction. Each week the patient receives one injection from a tuberculin syringe containing 0.15 cc. of this treatment extract, 0.15 cc. of a 1:20 dilution of mixed bacterial vaccine, 0.15 cc. of a 1:20 dilution of pertussis vaccine, and 2 minims of adrenaline. Injections are given weekly until there is definite improvement and then are given every 2, then 3 and finally every 4 weeks. However, each case must be individualized.

HAY FEVER IN CHILDREN

Pollen allergy is much more common in children than is generally realized and too often these children are treated for repeated "colds." Diagnosis can be established by correlation of symptoms with the pollen season, examination of nasal smears and diagnostic skin testing. Because of the usual low level of pollen skin sensitivity in children, the intracutaneous test is usually necessary, and tests should be done with all the common pollens in the environment. Specific desensitization therapy based on the history and skin tests is indicated in the manner previously outlined.

DERMAL-RESPIRATORY SYNDROME

Chairman Collins-Williams: The association of dermal allergy with respiratory allergy is so common that it may be referred to as the dermal-respiratory syndrome. In one large series of allergic children which we have studied 35% suffered from both dermal and respiratory allergy while under

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observation, and of those children who suffered from eczema, 59% eventually suffered from respiratory allergy. The practical application of this is that any child who has frequent severe "colds" and who has a history of eczema should be regarded as a potential case of respiratory allergy. If investigation confirms this, specific treatment should be started before severe respiratory allergy such as asthma develops.

Salient Diagnosis Problems in Asthma

Dr. Ratner: There are many causes of wheezing other than asthma and to make a correct diagnosis of asthma we must use all available means at our disposal including a careful history revealing especially repeated episodes of wheezing, precipitating factors, seasonal incidence and associated allergies; physical examination during the attack revealing wheezing accompanied by sibilant and sonorous rales; nasal smears; and fluoroscopy and roentgenography. Protein skin tests are then used to confirm specific etiologic agents. One must be especially on guard against misdiagnosing other correctable conditions such as foreign body.

Treatment of the Asthmatic Attack

The most serious errors in the management of the asthmatic attack are overmedication and an unfortunate choice of drugs. Subcutaneous adrenaline, 2 or 3 minims of 1:1,000 dilution, is the drug of choice. Syrup of ipecac to produce vomiting is indicated if there is not adequate response to adrenaline. Other treatment measures include propping up the patient, removal to another environment, circulation of air, steam, a cheerful attitude on the part of the attendants, intravenous fluids, rectal sedation such as bromide, phenobarbital or ether, oral sedation such as triple bromide, phenobarbital or seconal, and oxygen. Morphine and demerol should never be used.

Dr. Joseph H. Davis, Palo Alto, Calif.: In starting an elimination diet do you eliminate any skin reactors other than those indicated by history?

Chairman Collins-Williams: Any food incriminated either by history or by a positive skin test should be eliminated from the child's diet. If you start eliminating important foods such as egg, wheat and milk without valid reason you are going to deprive the child of foods which he needs for growth, and at the same time not help to relieve his allergic symptoms. However, as soon as the allergic symptoms are controlled, the forbidden foods are added one at a time to see if they can be tolerated.

Dr. Ratner: One of the most dangerous things is to deprive a child of a balanced diet. For that reason we like to use a denatured diet consisting of thoroughly cooked foods such as evaporated milk, well cooked cereals, boiled vegetables, stewed fruits, boiled meats and hard-boiled eggs. We believe that the boiling process greatly reduces the antigenicity of protein. Later we add unheated foods which the patient is not sensitive to, and later still small amounts of the offending allergens in nonheated form to see if they can be tolerated.

Dr. R. M. Matthews, Peterborough, Ont.: In connection with eosinophilia, is trichinella extract reliable for diagnosis?

Chairman Collins-Williams: Trichinella extract is reliable for past or present infection, but it does not give definite information about the present condition. For this reason trichinella extract has restricted value in diagnosis.

Dr. F. A. Olivieri, Toronto: You mentioned many conditions other than allergic rhinitis and asthma that caused eosinophilia. Do any of these conditions give rise to a local eosinophilia in the nasal secretion and other secretions?

Chairman Collins-Williams: As far as I know only respiratory allergy produces nasal eosinophilia with one exception—there is a transient nasal eosinophilia during the healing stage of an acute respiratory infection.

Dr. Ratner: I do not think that this problem has been studied well enough. It might be interesting to see if a case of trichinosis has a nasal eosinophilia. I do not think that anyone has done this.

Dr. Martin J. Harris, Louisville, Ky.: Are dilutions stronger than 1:5,000 ever used for desensitization therapy?

Dr. Ratner: Very few allergists use such low dilutions. Most use much stronger solutions.

Dr. J. S. Hunt, Charlotte, N.C.: Is the dosage of 1:5,000 pollen dilution decreased during the pollen season?

Chairman Collins-Williams: If you are using that dosage you ordinarily do not need to decrease

the dosage during the pollen season. However, if the child is having many symptoms you would be wise to cut it in half.

Dr. Davis: Is there any maximum number of pollens which you give in your treatment mixture? Cannot one pollen serve to desensitize for a group of pollens?

Dr. Ratner: Although some people feel that one pollen may be used to desensitize against a whole group of pollens, we feel that it is better to skin test the child with all the common pollens in the environment, and then to desensitize with all of them which give positive reactions. This is worth while as the treatment results are better.

Dr. C. L. Steinberg, St. Paul, Minn.: What is the longest interval used in perennial therapy?

Chairman Collins-Williams: I like to start by giving an injection every week. As soon as the patient is doing well these may be given 2 weeks apart, and finally as much as 4 weeks apart. This usually takes a long time, well over a year.

Dr. W. R. Whitely, Evanston, Ill.: You mentioned that you always give adrenaline in the same syringe as your desensitizing solutions. As all injections of diphtheria-tetanus and pertussis alum precipitated toxoid are given intramuscularly, would the administration of 1 to 2 minims of adrenaline delay the absorption?

Dr. John J. Miller, San Francisco, Calif.: I don't know whether adrenaline would delay absorption. Absorption is slow anyway.

Dr. Ratner: So, in that instance the adrenaline would serve as an antiallergic addition. Adrenaline definitely delays absorption for several hours.

Dr. Miller: Yes.

Dr. Thurman Shuller, McAlester, Okla.: Is there any place for histamine injection in the desensitization program?

Dr. Ratner: No.

Dr. Park S. Bradshaw, Muskegon, Mich.: For dust desensitization do you recommend an autogenous extract or a product like Endo housedust? What dosage do you give?

Dr. Ratner: For dust desensitization we recommend using a commercial preparation of housedust (Arlington Chemical Co.) which is mixed with the other indicated inhalants, pollens and molds, each in a 1 in 5,000 dilution.

I particularly recommend that the offending articles such as mattresses be covered with an impervious material like Egyptian cotton or Pima cotton or plastic, and that every attempt be made to reduce the dust content of the environment. This is sometimes a formidable job. Furthermore, visits to the attic, cellar, barn, etc., should be reduced and these places cleaned up as much as possible. Then desensitization procedures can be expected to be much more effective. The most brilliant results in all of allergy are obtained by the elimination of an offending substance.

Dr. Irving Weinstock, Brooklyn, N.Y.: In practice we find that allergic children are more susceptible to upper respiratory infections than normal children. Preventive injections of dust, vaccine, etc., are often not too successful. Why is this so and how do you treat this type of child?

Chairman Collins-Williams: It is true that allergic children are more susceptible to upper respiratory infections, but by means of the nasal smear it can be demonstrated that many of these so-called infections are in reality allergic manifestations. These cases should be handled as follows: (1) The nasal smear should be used routinely to determine which are infective episodes and which are allergic episodes. (2) Infective episodes should be treated early with appropriate chemotherapy, especially in the case of the asthmatic child whose acute asthmatic attacks are often precipitated by respiratory infections. (3) Allergic episodes should be treated with proper antiallergic symptomatic therapy such as an aminophylline-ephedrine-phenobarbital mixture. (4) The child should be skin-tested with the common inhalants, pollens and molds in his environment. (5) The child should be desensitized with those environmental allergens which give positive skin reactions and with mixed bacterial vaccine and the same allergens should be removed from the child's environment as much as possible. If this routine is always followed, the child will almost always show considerable improvement.

Dr. Alexander Kahn, Indianapolis: Are respiratory vaccines really useful and if so, what preparations are recommended in the treatment of the child with repeated respiratory infections?

Dr. Ratner: The question of the value of vaccine therapy is one that will be debated as long as we practice medicine. The truth is that we do not know how valuable they are. Most of us use stock

vaccines and think that they do some good. Autogenous vaccines have a limited value and the additional trouble and expense involved in their manufacture probably does not justify their use.

Dr. Howard Lange, Belleville, Ill.: What is the dosage and frequency of injection for bacterial vaccine?

Chairman Collins-Williams: I usually include 0.15 cc. of a 1 in 20 dilution of mixed bacterial vaccine in the same syringe with the desensitizing treatment extract for any child with respiratory allergy. These injections are given weekly until there is definite improvement in symptoms and then every 2 or 3 or 4 weeks as required. Many people use larger doses and this is quite justified provided one does not produce reactions.

Dr. Marcus E. Farrell, Clarksburg, W.Va.: What relationship is there between nasal and sinus infections and the onset of allergic symptoms?

Chairman Collins-Williams: Practically all allergic manifestations are made worse by bacterial infections and for that reason there is a close relationship between allergic manifestations on the one hand, and infections in the nose and paranasal sinuses on the other. For this reason it is important to clear up nasal and sinus infections, especially in the asthmatic patient.

Dr. Farrell: Is it practical to use sulfa prophylaxis in such cases?

Dr. Ratner: I think that this whole question of nasal and sinus infection is very important. Rather than using sulfa prophylaxis I prefer to evaluate each acute episode by means of the nasal smear. If the nasal smear is predominately neutrophiles, I begin oral antibiotic therapy immediately and thereby produce a recession of the infectious process which might lead to a nonspecific allergic episode. I prefer the use of oral penicillin or terramycin at these times, since I have seen a great deal of allergy to sulfa drugs.

Dr. H. E. Edwards, Toronto: Would you discuss the anemnestic reaction?

Dr. Ratner: The effect is produced by the development of various antibodies and the original work on the anemnestic reaction was with animals who were injected with 5 or 6 antigens. After an incubation period a nonspecific rise in antibodies of all the antigens could be elicited by an injection of any of the original antigens injected. So the anemnestic reaction may be nonspecific in action. If you take milk, feathers and eggs, and produce antibodies to each and give any one of those antigens at some later time there will be a small rise in antibody titer to all of them, but the greatest rise to the antigen you inject.

Dr. Jacob Rosenblum, Brooklyn, N.Y.: Would you please say a word about the Gay treatment?

Dr. Ratner: He is practicing a good type of psychotherapy. This is not enough in allergy if you are very much interested in the basic principles of medical practice.

Question: What is the incidence in an average practice of being able to cure a case of asthma by removal of the cat or dog or some other single item? I have rarely been able to obtain good results by doing that.

Chairman Collins-Williams: In my experience it is very rare to get a good result by doing that. Nearly all children with asthma are sensitive to many things. However, by making the child's room "dust-free" you can often help him a great deal.

Dr. Ratner: I would like to emphasize what has been said about control of the environment. We have had rather poor results with desensitization against dust and we think that best results stem from control of the environment. We just had a case of raw silk sensitivity and when we removed every bit of old silk from the environment we began to get a good result. Control of the environment produces the best results in the long run. It is the completeness with which the child is tested and the completeness with which these things are eliminated which spell success.

Dr. Davis: There has been some discussion in the literature that dog hair is not nearly as allergenic as cat hair and not as important to eliminate in the environment as it is other animals. Please discuss this.

Chairman Collins-Williams: This is going to depend a little on the history of the child. For example, if the child has seasonal asthma and has a dog to which he is very attached and does not seem to have any symptoms due to the dog, I think that it is all right for him to keep the dog. On the other hand, if he has severe asthma the year around, I think the dog should be eliminated from the environment.

Dr. Martin J. Harris, Louisville, Ky.: Do you adhere to the principle of prophylactic skin testing and treatment in children who have few symptoms but repeated growth of adenoid tissue?

Dr. Ratner: We do not do skin testing for this condition alone, but if an allergic child has residual or compensatory enlargement of the pharyngeal lymphoid tissue we sometimes have a reliable nose and throat specialist treat the pharynx with radium. It has value in certain cases.

Dr. Shuller: Where do antihistaminics fit into the management of hay fever and asthma in children?

Dr. Ratner: Antihistamines have provoked quite a sensation in medical practice in the last few years. They were presented to the lay public first and then to the doctors. They proved to be an interesting group of drugs that have antispasmodic properties and a tendency to dry the secretions. They are mildly palliative in allergy. Perhaps in the next few years we will not use them quite so much. Antihistamines do not get at the core of hay fever nor at the core of asthma. I might say here that at the present time everything is hitting allergy practice. There is a terrific swing toward ACTH and cortisone. Psychosomatic medicine has made inroads in the practice of allergy as well as the antihistamines. Some of us feel that after these things are tried for a number of years those people who have trouble will have more trouble and eventually will seek the advice of an allergist who is soundly concerned with the antigen antibody mechanism. We still think that that is the best approach to allergy and we like to think of allergy practice as the rehabilitation of the allergic cripple. Environments have to be corrected, certain foods have to be modified, certain immunities have to be built up and certain constitutional factors recognized. It is no different than our whole program of preventive pediatrics. With such care of the allergic child the majority of children who are willing to stay for a year or 2 are definitely rehabilitated.

Dr. H. Lander, Chicago: Have you had any experience with Dust-Seal?

Dr. Ratner: We have had some experience with it and we think it is begging the question of allergy. It is expensive and is not nearly as effective as ridding the environment of the dust-producing substances like cotton linters, old feathers, etc. It seems to me that we should try to eliminate these things rather than try to weigh the dust down with oil.

Dr. H. P. Fine, Perth Amboy, N.J.: How does dampness aggravate hay fever or asthma?

Chairman Collins-Williams: There are 2 ways it may affect it. First of all if a patient goes into a damp place he may come in contact with allergens to which he is sensitive, particularly molds. Secondly, many patients who have either allergic or nonallergic respiratory disease are worse in damp places. I do not know the reason for this.

Dr. W. R. Britton, Montgomery, Ala.: Spasmodic croup usually occurs late at night during sudden changes of weather. Is this not a physical allergy?

Dr. Ratner: It may be infection and it might be physical.

Dr. Howard J. Morrison, Savannah, Ga.: What is the average duration of the state of sensitivity to a particular food in infants and children as compared to adults?

Chairman Collins-Williams: I do not think that I can answer that fully. In general terms it is usual for an infant's food sensitivities to disappear during childhood though in an individual case the sensitivity may last into adult life.

Dr. Ratner: There may be instances when an individual is sensitive to sea foods, and if they are left out of the diet for one or more years they can be eaten without difficulty.

Everytime an infant takes a protein food for the first time he goes through a stage of allergy. As he takes that food repeatedly he goes into a state of immunity and that is why we feed foods cautiously because we know that the infant can bypass the state of allergy and go into a state of immunity. What actually happens is that as one takes food regularly, one becomes immunized.

Dr. H. Lander, Chicago: I have been impressed by the number of asthmas I see at the tail end of the hay fever season. Many of these patients are not hay fever patients. Is there some explanation of this and is it a common finding?

Chairman Collins-Williams: Are these mold cases?

Dr. Lander: No.

Chairman Collins-Williams: I think the answer to this problem is that the cases have not been adequately tested to determine all their sensitivities. Or, it may be that these patients are just developing new sensitivities and do not yet give positive skin tests.

Dr. Edwards: We have noted this phenomenon in Toronto this year and in going back over the cases we have been treating, we wondered whether it would be a good idea to include ragweed and grasses in the treatment extracts of these patients.

Dr. George H. Garrison, Oklahoma City: Would you discuss the indication and value of irradiation therapy over the chest in asthmatic individuals?

Dr. Ratner: I do not know anything about it, but I would be afraid to use it.

Dr. David R. Davis, Emporia, Kans.: Is ragweed dermatitis fairly common in children?

Dr. Ratner: Whether it is common or not it does actually occur and one must be alerted to it. If you get a positive skin test to a pollen and the dermatitis becomes aggravated during the pollen season, the pollen may be the cause of the dermatitis.

Dr. Charles J. Eldridge, Kansas City, Mo.: Will you discuss the dietary treatment of infantile eczema before skin tests can be made?

Dr. Ratner: For many years we have used a denatured diet consisting of boiled milk, boiled eggs and thoroughly cooked foods of all kinds.

Dr. Philip J. Panitz, Akron, Ohio: How often does breast milk produce eczema or other allergies?

Dr. Ratner: Is this eczema of the face to which you are referring?

Dr. Philip J. Panitz, Akron, Ohio: Yes.

Dr. Ratner: That may not be an eczema, but may be due to contact dermatitis with the mother's breast. I disagree with Dr. Collins-Williams' attitude that a breast-fed baby with eczema should be left on the breast. I don't believe that breast milk is as reliable a food as he seems to think. When it is good breast milk it is the best food obtainable, but when it is bad breast milk it is a poor food.

Dr. W. Eugene Keiter, Kinston, N.C.: Is the pulse rate in food sensitivity testing an indicator of sensitivity?

Dr. Ratner: Dr. Coca claims that the pulse rate is increased when you have food intolerance, but we have been unable to try it out in children because their pulse rate is always shooting high.

Dr. George H. Garrison, Oklahoma City: Of what value are repeated white blood counts (every 15 minutes) after feeding a suspected food?

Dr. Ratner: That is the leucopenic index and has been abandoned.

Dr. M. B. Low, Greenfield, Mass.: What proportion of your allergic children do you treat for hypothyroidism?

Dr. Ratner: Just those that show evidence of hypothyroidism.

Dr. M. C. Carlisle, Waco, Texas: Is ether per rectum of any value in status asthmaticus?

Dr. Ratner: The answer is yes. It has great value and you give about 2 or 3 teaspoonfuls mixed with 2 ounces of olive oil as a retention enema. It does have a satisfactory effect in some cases and in others it does not.

Dr. Nathan Goluboff, Saskatoon, Sask.: Do you find isuprel® or other types of inhalers of much value? Have they any dangers in repeated use in asthma for symptomatic relief?

Chairman Collins-Williams: The inhalers are of use if used properly. The difficulty is that they are apt to be used too often particularly by the older child who uses an inhaler himself. There is therefore a great danger of overdosage, whereas if you prescribe some type of oral medication the mother is more apt to keep to the dosage prescribed.

Dr. Ratner: I think, too, that the use of inhalers has a tendency to produce an addiction. With benzedrine inhalers those people who once begin to use them often keep it up. It gives a lift and for that reason we think that a remedy which is so easily available results in psychologic dependence.

Dr. Joseph H. Davis, Palo Alto, Calif.: Is intravenous epinephrine liable to be lethal?

Dr. Ratner: The use of intravenous adrenaline perhaps might be lethal or dangerous. I might say this, large doses of adrenaline are ill advised. If you give 1 or 2 minims you are getting the best physiologic reaction. But, if you give more than that it causes vascular reactions with a rapid pulse, pounding headache, syncope and further constriction of the bronchioles. The patient has a reaction which is worse than the asthma for which he was treated.

Dr. Arthur J. Cramer, Buffalo, N.Y.: What value, if any, for the treatment of asthma are the following: pyromen or diethylene sulphonate?

Dr. Ratner: Pyromen is thought to act like cortisone and some men are trying it out. Diethylene sulphonate is an absolutely spurious medication. It has been proved that it has no value whatsoever and it is equivalent to triple distilled water.

Dr. Alexander Kahn, Indianapolis: Is adrenaline in oil a useful preparation in treating acute asthmatic attacks? What dosage do you recommend?

Dr. Ratner: Oil should never be used for the simple reason that you get an oleoma which may necessitate removal of a large tumor mass produced by the oil.

Chairman Collins-Williams: I do not use the oil for that reason and also because you cannot expect a better result with adrenaline in oil than with the same dosage of aqueous adrenaline. It is better to give 1 or 2 minims of adrenaline and repeat it, rather than ½ cc. of the oil which is the usual dose.

Dr. Philip I. Panitz, Akron, Ohio: Do you recommend the use of a combination of oxygen and steam such as in the croupette for asthma?

Chairman Collins-Williams: I certainly do recommend the use of oxygen and steam as in the croupette for the severe asthmatic attack. However, there is one danger in the use of oxygen in the severe attack. After a prolonged attack of asthma the patient is suffering from respiratory acidosis due to carbon dioxide retention. The respiratory center, the main stimulus for breathing, may finally become poisoned by the carbon dioxide. The main stimulus for respiration then falls on the aortic body, which responds mostly to anoxia and very little to high levels of carbon dioxide. Therefore, the oxygen, by raising the oxygen content of the blood, may abolish the chief stimulus to respiration, and the patient may stop breathing. For this reason, when you put a severely ill asthmatic into oxygen you must watch him and take him out immediately if he stops breathing. This chain of events does not happen often, but is something which we must bear in mind.

Dr. Ratner: The reason we like to give steam along with the oxygen is that the asthmatic child has tremendous dehydration of the respiratory tract.

Dr. F. A. Olivieri, Toronto: Have you had any cases of asthma made worse with rectal seconal?

Chairman Collins-Williams: I have not had any cases, but large doses will make the child very much worse.

Dr. Ratner: That is an important question because that type of drug is the thing that might kill the child. Sedatives like seconal are fairly safe, but I think it is better judgment to use small doses of these—¼ grain of phenobarbital, ¼ grain of seconal. Don't give a child a knockout blow, for the harder he breathes and the more fight he has in him, the better off he is.

Pediatrics

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SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

"A forum where discussion could be free, intelligent and continuous."

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

COMMUNICATIONS FROM SHIMON BERMAN, M.D., AND S. Z. LEVINE, M.D.

The first communication describes the teaching of pediatrics in the new State of Israel. It is written by Dr. Shimon Berman, who has worked in various departments of pediatrics in this country and who is now professor of pediatrics at the Hadassah University Hospital in Jerusalem.

The second communication, by Dr. S. Z. Levine, describes his observations on pediatrics in Israel as a member of a medical mission there in September 1951.

PEDIATRIC EDUCATION IN ISRAEL

IN A recent issue of this journal Dr. J. H. Ebbs (PEDIATRICS, vol. 4, no. 8, p. 563, October 1951) gave an account of pediatric education in Canada. This article described the gradual evolution of pediatric activities and education in a well ordered, stable and prosperous community. While pediatric activities were no doubt modified in many details in Canada to conform with the special needs of that country, in their general features they are similar to those in Western Europe, Great Britain, and the United States. This is likewise true of pediatric education in Canada. Israel, on the other hand with its unique history and its peculiar problems, illustrates the manner in which pediatric activities, among which teaching must be included, are influenced by the ways in which a society came into being, its composition, and the pattern which it possesses.

Pediatric Education During the Period of the Mandate

Shortly after the capture of Jerusalem in 1917, Hadassah* sent a medical mission from the United States to Palestine. This mission opened a number of infant welfare stations in the country and began with an organized campaign against trachoma which was then, as now again, widely prevalent. At the beginning of the British Mandate the Jewish population numbered about 80,000; at the end of the Mandate in 1948 it had grown to 650,000. This growth was due largely to immigrations; the majority of the newcomers were of a high cultural level and came mainly from Eastern Europe up to 1933, when a large immigration from Central Europe began which ceased only at the outbreak of the Second World War. Although Jews of European origin were in the majority there was a big minority group of Oriental Jews. The European Jews demanded a high level of pediatric services and utilized to the full the facilities first provided by Hadassah and later supplemented by various local medical organizations, municipal and Kupat Holim (sick fund of the General Federation of Labor.—Ed.). These facilities were tendered the Oriental Jews and the Arabs as well and were taken advantage of, after a lag of many years, to a rapidly increasing extent. It is to these services, especially the pre-natal and infant welfare clinics, that we can ascribe the relatively low infant mortality which reached the gratifying figure of 32 per 1000 live births for all sections of the Jewish Community in 1947.

In the 1920's with the opening of Jewish hospitals in the country the number of pediatric departments grew. No matter how small the hospitals were, they had their children's departments which comprised 20 to 30% of the total beds and which were under the direction of pediatricians who had received their training usually in Central Europe. Young doctors served as house physicians and later as assistants in the children's wards, receiving what was in the nature of a loose apprenticeship form of training. There was no planned graduate teaching of the younger men and no fixed number of years was required for specialization. After a variable period in the hospitals, usually no less than two years, but at times 10 years and longer, these men specialized in the practice of pediatrics only. Many of them, even those with shorter experience in the hospitals are now reliable practicing pediatricians, while some with much hospital experience are now heads of pediatric wards and are in turn training a new generation of physicians.

A definite advance in the quality of graduate teaching of pediatrics occurred in 1942, when one of the hospitals added preventive pediatrics as an integral part of the work of the house physicians and assistants. It was realized that the hospital department was only the center, that from this center activities should radiate outwards and serve and influence all aspects of Child Health in the community as well as being influenced by them. The head of the department in the hospital also supervised the infant welfare work of the parent institution and his house men and assistants were put in charge of one or more infant welfare stations in addition to their work in the wards. This has been so successful that the Department of Health of the State of Israel has accepted it as its policy that every hospital department in the country must be responsible for all child health work in the area surrounding it, a policy to be implemented as soon as conditions allow.

* Hadassah is a women's organization in this country which supports medical and social welfare in Israel—Ed.

On a postgraduate level this had been implemented in lower and upper Galilee. A hospital is located there in the midst of many agricultural settlements. For over 20 years the pediatrician in this hospital has been visiting each settlement once a month and together with the general practitioner sees those children that the latter presents to him. The pediatrician acts as a consultant and as an instructor to the settlement doctor and nurses. All pediatrics work in the settlements is done by the local medical personnel and as the result of the monthly visits of the pediatrician they quickly learn to do it well. Unfortunately, another system was introduced in the rest of the country; there the pediatrician visits the rural settlements once a week or once a fortnight, and without the local doctor sees all the children brought to him by the parents. He or some other visiting doctor may conduct an infant welfare clinic in the same village. The general practitioner not being associated with the pediatrics work, child care in all its aspects suffers in these places.

Finally in those hospitals which had a rotating interne service, this included three to four months' work in the children's department. Furthermore, all hospitals readily accepted into their departments visitors for varying periods. If these visitors came for longer than a week an attempt was made to integrate them into the routine work of the wards.

Pediatric Education in the State of Israel

On May 15, 1948 the State of Israel was proclaimed. Shortly afterwards mass immigration began; the remnants of the Jewish communities of Central and Eastern Europe, the inmates of the D.P. Camps; immigrants from North Africa, from Yemen, Iraq and other countries of the Middle East. From some countries this constituted a total exodus of the Jews, men, women and children; old and young, the well and the ill. In the few years of its existence Israel's population has grown from 650,000 to approximately one and one half millions. All cultures are represented from the primitive cultures of the Jews of Yemen or of Kurdistan, through the transition cultures of parts of North Africa and Iraq, to that of Europe and the English speaking countries. The bulk of the recent immigrants are from North Africa, Yemen and the Middle East. They often have many children and must be taught the first principles of hygiene and child care. Moreover, so large an influx of new immigrants which have to be housed, integrated into the economy of the country and looked after in health and in disease has created a host of problems. Living conditions are still inadequate, hygiene is poor in many places, and the resulting morbidity among infants has put a strain upon all existing medical services especially in the field of pediatrics. The immigrants constitute Israel's major problem and will continue to do so for a number of years to come.

Among the immigrants were a number of medical students who had interrupted their studies to come to Israel. An additional number of Israelis studying abroad had returned to participate in our War of Independence. When hostilities ceased, faced with the problem of what to do with these two groups of students, undergraduate medical teaching was begun in Jerusalem on April 10, 1949 and in November of that year the first group entered the wards of the Hadassah University Hospital for their clerkship in pediatrics. The students having completed part of their undergraduate work before returning or coming to Israel, our newly opened Medical School began with the second pre-clinical and the clinical years. We hope to start first year medicine this year.

Undergraduate teaching is modelled after the American and British systems, with

small groups and individual instruction. No other method of instruction would have been successful, for our students are a heterogeneous group coming from many schools with a varying quality of preparation. Only individual instruction is therefore possible and after a year or so most of them become welded into a group, the individual members of which are much more of a comparable level scholastically. We are introducing a sort of tutorial system into our pediatrics clerkship; each member of the staff is given three students for whom he will be responsible and whose daily progress he will supervise. The tutor will acquaint himself with the individual weaknesses of his students in the pre-clinical sciences as far as they are basic to pediatrics and will endeavor to remedy them.

Out students have a two months' clerkship in the wards during their first clinical year and an additional month in their second, when they also have a month in the out-patient department. Before entering upon their clerkship in the major departments they have already had courses in physical diagnosis, clinical pathology and short courses in neurology, eye, ear, nose and throat, and dermatology where they are taught the fundamentals of examination of the patient in the various specialties. They are, therefore, expected to possess the necessary techniques, and a complete physical and laboratory examination of cases is required of them from the start. Ward rounds, case presentation; conferences, clinical pathological, X-ray and childhood tuberculosis, and talks on selected subjects constitute the routine of teaching. The physician on duty in the department has two students, in rotation, to assist him. Systematic didactic teaching is given in the first clinical year in the form of one lecture a week. Hebrew is, of course, the language of instruction, but the recommended textbooks and periodicals are practically all in English.

Teaching as well as learning possessing direction as well as magnitude, it has been our aim in all undergraduate teaching to give it the direction of public health and preventive medicine. So much of pediatrics possesses this direction and it should, therefore, be implemented most easily and most thoroughly in this specialty. When one attempts to do so, however, many difficulties are met which had not been foreseen.

We planned to teach those parts of public health which dealt with infants and children in full, both didactically and by means of practical demonstrations. We also planned to stress the public health aspects and implications of the diseases encountered in infancy and childhood. Much preparation and time will be required, however, before we even begin to realize our plans. Up to now we have only touched upon the subject of public health pediatrics. We have included visits to the infant welfare stations in our courses, visits to immigrant camps and settlements, to youth immigrant institutions. Rehabilitation of poliomyelitis victims, and the psychological and social aspects of the care of tuberculous children have been touched upon. To some extent we have been able to include the public health or preventive medicine aspects of the subjects treated in our seminars and of the cases lying in our wards. We are not afraid that curative pediatrics will be neglected through over-emphasis of the public health and preventive medicine portions of the subject, and we, therefore, hope to widen the teaching of the latter. We would like our undergraduates to come to the conclusion that pediatrics aims to care for the period of growth and development in a manner to assure optimum health during infancy and childhood and to ensure healthy adulthood in the future.

Good teaching of any subject requires that it be well taught on all levels; that in addition to undergraduate, postgraduate and graduate teaching be developed. Moreover, we believe that it is desirable to institute the teaching of the subject simultaneously on

all the levels for we feel that they are closely interrelated. If for any reason this is neglected, or is impossible to realize, deterioration of what teaching is being done is likely to result. We think that of all subjects in medicine public health and hygiene are modified most by local conditions and pediatrics next. The basic training in these subjects even on the graduate level should, therefore, be obtained locally and the facilities for this must be created.

We have not yet done much in postgraduate teaching of pediatrics and we believe that there is a pressing need for this. We should like to see that every rural physician gets a good basic course of two months in pediatrics with shorter refresher and supplementary courses subsequently. He will then return to his work better equipped to do all routine pediatrics including infant and child health work. If specialists will be available they will visit the settlements at intervals as teachers of and consultants to the local physicians. Furthermore, there should be close contact between the pediatric department and the physicians in the area. This will be possible when the work in the hospital department and that in the surrounding district from which its patients are drawn complement each other.

Graduate teaching of pediatrics should be of two varieties: one to train men to be practical specialists, and the other to train teachers of the subjects. While that latter may emerge from the former, we think that better results could be obtained through systemized planning of the training of teachers of pediatrics.

The training of specialists has continued along the lines described elsewhere. The Israel Medical Association and the Pediatrics Society of Israel now demand four years' residency in an approved hospital for specialization in pediatrics. Undergraduate teaching has also influenced the teaching of the house-physicians and assistants in that the latter are brought into close contact with the basic medical sciences. Specialist examinations have not yet been initiated in Israel, but there is no doubt that this will be done in the near future, both of men trained here and those who have had their training elsewhere and have come to Israel to practice their specialty. Specialist status granted by other countries will be recognized in Israel.

The training of men destined to be teachers of pediatrics must be more basic and wider in range. In general what we had planned is similar to that which has been instituted in Canada and possibly elsewhere. Believing that a teacher of undergraduates in a clinical subject must not only know his subject well he must have a good knowledge of at least one of the basic sciences; believing also that pediatrics and internal medicine being so closely allied in many respects a reciprocal acquaintance with each other's field benefits both the internist and the pediatrician, we made our plans accordingly. After about a year and a half in a pediatric department the candidate will work for a year in internal medicine. He will then receive about nine months' review of the basic sciences stressing those aspects which have an application in pediatrics. Subsequently he will be allowed to study and/or do research in one of the sciences for another nine months to a year, to be followed by a final year in the department in the hospital. We hope to be able to realize this plan with modifications, which will inevitably be forced upon us by circumstances.

The Jewish community has always demanded a high level of pediatric services both in the cities and in the rural areas. Pediatrics has always been, therefore, one of the major fields of medicine in this country. Israel is continuing this emphasis upon child health.

Consequent upon mass immigration infant and child morbidity has increased considerably; infant mortality has also increased but less than morbidity. The pediatric problems of the country are among the most important and most pressing and will continue to be so until considerable progress has been made in assimilating the immigrants. The growth of existing children's departments and the establishment of a number of new ones have helped to keep child mortality at a level which is low compared to morbidity. Increasing emphasis will have to be placed, however, on public health and preventive pediatrics. Services in all fields of child health will have to be established for all sections of the population, for the cities and the villages and for the many immigrant camps and settlements.

In the light of these conditions and needs pediatric education is carried out or planned. Both in undergraduate teaching and interne services the time devoted to pediatrics is generous and will probably be lengthened somewhat in the near future. A beginning has been made in teaching the public health aspects of the subject but this will have to be amplified considerably. We shall have to institute postgraduate courses in the essentials of pediatrics for rural physicians with refresher courses at intervals. The training of specialists is being organized to meet minimal requirements, but the number of places for house physicians and assistants will have to be increased. When the Government Department of Health implements its plans to make every children's department responsible for the child health services in the area, these departments will require additional staff and thus opportunities for training in pediatrics will become more numerous. A network of pediatric services will then be established from which every child in the country will be able to benefit.

In order to realize these projects we must have a larger number of teachers of pediatrics. These should receive their training here for we need Israeli pediatricians who know the problems of child health in Israel intimately and at first hand. We must, however, avail ourselves of training elsewhere especially in special subjects, but this should follow upon and not substitute for the fundamental training in Israel. The immigration of specialists who have received their training in other countries as well as the visits of prominent pediatricians from abroad will constantly enrich our knowledge and skills and will ensure continued harmony with world pediatrics.

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PEDIATRIC IMPRESSIONS GAINED ON A MEDICAL MISSION TO ISRAEL

IN THE last four years, the World Health Organization (W.H.O.) of the United Nations (U.N.) and the Unitarian Service Committee (U.S.C.) of the United States have, at the invitation of the respective governments, sent joint medical teaching missions to Austria, Poland and Finland, the Philippines, and Israel and Iran. An official agency of the government, usually the Ministry of Health, initiates the project by presenting an agenda of needs. If approved, the two sponsoring agencies with the aid of a joint preparatory committee then plan the time table, content and personnel of the missions. Although tailored to meet individual needs, the over-all purposes served by these missions are threefold: (1) as a forum for discussion of the health needs and problems of

medical education in the host country; (2) as a medium for supplying medical books and equipment; and (3) as a means of making personal contacts and cementing friendly relations with foreign medical colleagues. Such health programs contribute much to friendly international relations and they merit wide circulation and support.

The mission to Israel took place in September 1951. The special areas on which the Director General of Health, Dr. Chaim Sheba, asked coverage were: (1) exchange of information in the basic and clinical sciences and public health by formal lectures and demonstrations, rounds, seminars and conferences; (2) advice on and instruction in public health matters; and (3) consultation on problems of medical education. With these areas in mind, W.H.O./U.S.C. selected the following scientists, clinicians, educators and public health workers as members of the mission:

Dr. Leo M. Davidoff, Chairman, New York City—Neurosurgery
Dr. Karl Evang, Vice-Chairman, Oslo, Norway—Public Health
Dr. John E. Gordon, Boston—Epidemiology
Dr. E. Grzegorzewski, Geneva, Switzerland—Medical Education
Dr. Paul Klemperer, New York City—Pathology
Dr. Samuel Z. Levine, New York City—Pediatrics
Dr. Gordon K. Moe, Syracuse, N.Y.—Physiology and Pharmacology
Dr. Lucien E. Morris, Iowa City, Iowa—Anesthesiology
Dr. H. Osmond-Clarke, London—Orthopedic Surgery
Dr. Leo G. Rigler, Minneapolis—Radiology
Dr. Carl Semb, Oslo, Norway—Surgery
Dr. Hugo Theorell, Stockholm—Biochemistry
Dr. Richard G. Tyler, Seattle—Environmental Sanitation
Dr. Erik Warburg, Copenhagen—Internal Medicine

Dr. Erwin Kohn, Chief of Scientific Exchange Section of W.H.O., Dr. Edward Grzegorzewski, Director of Division of Education and Training Service of W.H.O., and Mr. Howard L. Brooks, Associate Director of U.S.C., served as advisors and administrative officers of the mission.

To serve as pediatrician of the mission was especially gratifying because the young State of Israel had, as basic governmental policy, given highest priority to the health and education of its children. All official and voluntary health agencies are dedicated to this principle: Ministry of Health, District Health Offices of the Government, Municipal Health Services, Army Medical Service, Kupat Holim of the Histadrut (Sick Fund of the General Federation of Labor), the Israel Medical Society, the Hadassah Women's Organization, the Women's International Zionist Organization, and physicians engaged in private practice. At great sacrifice to the adult population and in the face of extreme shortages of food, shelter, professional personnel, and medical supplies, every effort is being made to promote the health, growth, and literacy of the next generation of citizens.

In actual practice, this goal has understandably not yet been attained. Although the ratio of doctors (3,300) to population (1,600,000) is high (1:500), many physicians are old and infirm (their mean age is 55 years); others have been deprived of the opportunity to keep abreast of modern trends in medical practice and, as in other countries, they tend to concentrate in the large cities of Tel Aviv, Haifa and Jerusalem. Well-trained pediatricians are scarce, especially in rural areas; pediatric nurses are in short supply; there is a dearth of social workers and teachers. In the face of this paucity of skilled

pediatric personnel, great hordes of impoverished immigrants with their sick and malnourished infants and children have been pouring into the country in the last three years at the rate of 18,000 or more per month. The population has more than doubled in this period. In 1951 alone, over 200,000 refugees (more than half without previous training in agriculture, industry or the professions; and somewhat under one-third, children below 15 years of age) have migrated from Iraq, Rumania, North Africa and other countries and the stream of immigration is not yet ended. About 400,000 more are expected in 1952 and 1953. In its Proclamation of Independence, the Government declares: "The State of Israel will be open to the immigration of Jews from all countries of their dispersion."

Separation of the well from the sick in reception camps, placement of the well in settlement camps (Maabaroth), and accommodations for the sick in hospitals are monumental tasks in a country as young (proclaimed a State on May 14, 1948), as small (8,000 sq. miles in area), and as poor as Israel.

Despite the difficulties, screening and immunization procedures in the reception camps are conducted promptly and well. Except for infantile poliomyelitis in epidemic form in 1950, the spread of other serious epidemic diseases has been successfully prevented. Persons free from infectious disease are dispatched to transient settlement camps and assigned to canvas tents vacated by older occupants who had been promoted to tin and then wood huts. These camps number around 175, house a total of nearly 200,000 immigrants and are spread throughout the country. Each contains from 100 to 1,000 families. In one camp that I visited, consisting of Kurd and Iraq Jews, 1,000 of the 1,350 dwellers were infants and children.

Even though efforts are made to provide health, school, and social services, conditions in the settlement camps are difficult. The enormous influx of infants and children from the underprivileged countries of the Middle East and North Africa, the high birth rate in the Maabaroth, the unsanitary conditions all contribute to a high infant morbidity and mortality. Food and often water are insufficient, means for their refrigeration are lacking; flies are plentiful and the few latrines unclean. Superimposed on these primitive conditions are the absence of any knowledge of hygiene and often the presence of harmful superstitions of the newly-arrived inhabitants. One Israeli doctor, a pediatrician and head of a large hospital service, describes conditions in the following way:

"Camp doctors are general physicians and have no pediatric experience. Many infants are underfed and they are readily overcome by infections, and so the bulk of our pediatric hospital admissions are infants with malnutrition, gastroenteritis and toxicosis, frequently of infectious etiology. Tuberculosis is common and pneumonia a frequent complication. Children are sent to a hospital after having endured long distance transport and may find no available bed on arrival, so they are referred from one hospital to the next before a vacancy is found." Another camp physician told me that of 5,000 children under his supervision, 55% of cases seen by him for treatment comprised ophthalmologic and dermatologic conditions. "Virtually all the children under two years of age are suffering from malnutrition, many with diarrhea and tuberculosis, and the rest have ringworm and trachoma. Many children are hurt or even die from accidents." It is easy to understand why the infant mortality rate which had fallen from 135 deaths per 1,000 live births in 1925 to 32 in 1948 has again risen to 63 in 1950. The subsequent decline to 56 for the first six months of 1951 gives promise of further improvement. The birth rate mean-

while has risen from 30 per 1,000 population in 1949 to 33 in 1950.

In contrast to the prevalence of infantile malnutrition existing in the Maabaroth, the infants in the Kibbutzim (collective farms comprising about 40% of all agricultural settlements) which I visited were in robust health and well cared for and fed in communal crèches. The chief medical problems with respect to children are very different in these old established settlements than in the transient settlements for immigrants; namely, the high incidence of cross-infections, and the feelings of rejection which may arise from physical separation of infants and children from their parents. The impression I had was that in general this psychological hazard may be expected to be minimal and that it is fully compensated by the affection showered by parents and the adult population of the Kibbutzim as a whole on their infant population.

Pediatric practice in the hospitals of Haifa, Tel Aviv, Affula and Jerusalem is of high caliber. The chiefs of service are well trained, they have kept abreast with modern trends in pediatrics and the younger staff members are able. The medical staffs are, however, handicapped severely by shortage of qualified assistants, especially laboratory technicians and secretaries, by inadequate laboratory facilities, by the dearth of nurses and social workers and by overcrowding in the hospital wards and outpatient departments. To make room for the constant flow of new admissions, children are discharged before they have completely recovered, frequently to return to the stringent conditions of camp life. There are too few children's convalescent homes and rehabilitation centers. The need for expanding outpatient facilities is similarly urgent. Ambulatory patients, including infants and children, begin to queue up in the early morning and many are not seen till late afternoon.

Besides the usual ailments treated in children's hospitals in the United States, the bulk of the remaining hospital admissions comprise infantile diarrhea and marasmus, diphtheria and other childhood contagious diseases, poliomyelitis, tuberculosis, "spastic bronchitis," certain parasitic diseases (schistosomiasis, malaria, kala-azar), favism, and blood dyscrasias which seem to be limited to Jews of Oriental origin. It is remarkable that, in the face of all the difficulties, the pediatric wards in the many hospitals I visited throughout Israel were clean and orderly, the children were well fed and provided with recreational facilities, the medical work-ups were thorough, and the hospital records well kept. Curative medicine in pediatrics, both with respect to diagnosis and treatment, is well practiced.

What is needed, in terms of long-term planning, is the expansion of preventive programs for preserving and promoting the physical, mental and emotional health of children. Official and voluntary agencies are well aware that existing programs, hitherto adequate for the natural increase in native population, are now insufficient for the immigrant load. Not only do general public health, epidemiologic and environmental sanitation measures need strengthening but, more specifically in terms of child health, greater attention must be given to food rationing, dairy inspection, milk pasteurization, immunization procedures and control of communicable diseases, BCG vaccination, accident prevention, and maternal and child health centers.

Because of the scarcity of well-trained pediatricians and, for that matter, all physicians, the problems of medical education assume great importance. The only medical school in Israel (The Hebrew University-Hadassah Medical School) is one of the 12 or more colleges of the Hebrew University in Jerusalem. This center of learning was housed in

magnificent buildings on Mount Scopus until 1948. Following a forced evacuation, the medical school and affiliated hospitals are now relocated temporarily in old and converted buildings scattered throughout the new city itself. A new site for a unified medical center has already been selected in the western section of Jerusalem, building funds have been made available by the Hadassah Women's Organization, blue prints are in the preparatory stage, and the new center is expected to begin operations in the next four or five years.

In the meantime, the medical faculty is striving to overcome the many obstacles which stand in the way of effective instruction. The pediatric department consists of a ward of 50 beds in a converted building, an overcrowded outpatient division, a small lecture room, and inadequate laboratory space. The recent appointment of an American-trained pediatrician, Dr. Shimon Berman, to head up the undergraduate teaching program in pediatrics has stimulated interest and enthusiasm in the student body. He is a highly qualified clinician and excellent teacher and has gathered around himself a younger staff of able associates, two of whom are also American-trained.

The curriculum in pediatrics is well planned and the teachers are interested and competent, but the list of deterrents to effective teaching is large. Emergencies frequently arise which interfere with the actual conduct of teaching and the continuity of research. Faculty members may be commandeered from their teaching duties and assigned to man transient settlement camps or rural hospitals or to military service. Although understandable in terms of the over-all needs of the country at large, immunity of the faculty from these assignments could be a boon to the medical school. As in other countries, promotion to senior academic posts seems to depend primarily on qualifications for research and not enough on teaching interest and competence. Before 1948, the leading physicians were older men of distinction and achievement who had migrated from oppressed areas of Central Europe. This has led to a top-heavy distribution of elders on the faculty and to diminished opportunities for advancement of the younger staff members in terms of intellectual satisfaction, titular recognition, and financial emolument. Top full time salaries are low and inflationary trends have inordinately raised the cost of living. The salaries of younger staff members are less than the wages paid to the carpenter, the bricklayer, the taxi driver, and not enough for decent food, shelter, clothing, and recreation. As one of the staff stated it: "A man can get along in academic medicine if working conditions are good even if his salary is low, or he can get along with some intellectual frustrations if his economic condition is good, but he cannot be expected to be productive if he has neither adequate teaching and research opportunities nor a decent economic existence."

Another handicap to medical teaching is the poverty of the students. Many are underfed and have to do outside work to support themselves. Language difficulties aggravate other problems. The national language is Hebrew but students who have migrated from other lands (60 countries) may know only their native tongue. In most of the hospitals I visited, the staff members in the pediatric department alone comprised assorted emigrés from Germany, Poland, Russia, Czechoslovakia, Rumania, Hungary, England, South Africa, the United States, in addition to an occasional native-born (sabra).

In a country less impoverished than Israel, it would be simple to pay higher full time salaries to the faculty and provide free tuition, food, lodgings, and proper study conditions to promising students. This solution is of course currently impossible when the government is confronted with more pressing economic problems.

In the face of the formidable obstacles confronting the young state of Israel, and they are many, one cannot return from a visit to that country without a feeling of optimism at the heroic efforts, the abiding faith, and the outstanding achievements of the Israeli people. One is left with no doubt that the challenges in public health, medical practice and medical education which now confront the young State of Israel will also be met successfully when one sees the miracles of desert reclamation, land cultivation, afforestation, swamp drainage, water irrigation, road construction, and home building that have already been accomplished.

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TRENDS

By JOHN P. HUBBARD, M.D., *Contributing Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

In view of the importance of accidents as the leading cause of death in children, and in view of the increasing attention which pediatricians are giving to accidents, the following contribution has been submitted by C. Collins-Williams, M.D., Hospital for Sick Children, Toronto. This article calls attention to a campaign against accidents in children being conducted by the Health League of Canada, a voluntary agency whose purpose is the promotion of national health.

ACCIDENTS IN CHILDREN IN CANADA

ACCIDENTS, at the present time, are one of the principal causes of death, particularly among children. In Canada approximately 1,500 children die each year as the result of accidents, a mortality greater than that due to the 10 acute infectious diseases of childhood combined. During the five year period 1942-46 inclusive, in Canada, accidents stood in eighth place as a cause of death during the first year of life, in third place during the second year, and in first place during each year after infancy up to the fifteenth birthday. During the same period, 21% of the deaths between the first and fifteenth birthdays were due to accidents.

In this age of preventive medicine when our chief purpose as physicians is the prevention of morbidity and mortality, we, as pediatricians, cannot neglect this extremely important phase of child care. In any campaign to reduce the number of accidents, there are three ways in which the physician can play an important part. Firstly, the general public must be made aware of the seriousness of the situation and must be educated in the ways in which they, as citizens and parents, can help to reduce accidents. Secondly, the medical profession, working through its associations and publications, must stimulate all physicians to a concerted effort to reduce the number of accidents. Finally, and most important, the physician must concentrate on an educational program for his own private patients. A few words from the physician who looks after the child will do more to impress parents than will reams of propaganda published by someone unknown to them.

During the past year an educational program based on these three premises has been started in Canada. In the field of public education, three articles have been published in *Health Magazine,* the official organ of the Health League of Canada. This bimonthly publication is admirably suited for the purpose because, although its circulation is relatively small (25,000), it is widely quoted by the press and radio throughout the country. The first article, "Protect Your Children,"[1] emphasizes the number of accidental deaths each year and points out that these represent only a small fraction of the serious accidents which occur, most of which are nonfatal and therefore nonreportable. The common types of accidents which happen to children—poisonings, burns, cuts, falls, wringer injuries, electric shocks, ingestion or inhalation of foreign bodies, wounds due to firearms, traffic accidents, and drownings—and some practical measures for preventing them are described. The second article, "Save the Children,"[2] discusses the same kinds of accidents and describes what the parent should do as emergency measures for each type of injury

until a physician can be obtained. The third article, "Poisonings in Children,"[3] concentrates on poisonings, the sixth most common cause of accidental death among children in Canada, and the one which the alert parent can probably do most to prevent. This article deals with the most common poisons, describes ways of preventing children from ingesting them and lists the specific first aid treatment for approximately one hundred of them.

In addition, articles on accidents in children are now being prepared by two of the best known popular magazines with wide circulation throughout Canada. As these are being written by the magazines' own feature writers, their content is not known at the present time. However, these articles, which will reach a large audience, can be expected to contribute a great deal to education of the public.

In the second phase of the campaign, namely, bringing the seriousness of the situation to the attention of the medical profession as a whole, an article has been published in the *Canadian Medical Association Journal*.[4] This is a statistical review of the causes of death in children in Canada during the two five year periods 1922-26 and 1942-46, inclusive, analysed according to cause of death and age at death with a detailed breakdown of the accidental deaths. Among other things, these statistics show that in the period 1922-26 accidental deaths were in seventh place as a cause of death in children from birth up to the fifteenth birthday and that in children over the age of one year, 11% of the deaths were due to accidents, whereas, for the period 1942-46 the corresponding figures were fourth place and 21%. Study of the tables reveals that this increased relative importance of accidents is due in large part to a decrease in the number of deaths from the acute infectious diseases of childhood, tuberculosis, the other infectious diseases and diseases of the respiratory, circulatory, nervous and digestive systems, rather than to a great increase in the number of accidental deaths.

When the statistics are adjusted to the increase in population it is found that between these two five year periods there has been a reduction of 45% in the total death rate, whereas there has been a corresponding reduction of only 12% in the accidental death rate. These figures show how our conquest of deaths due to accidents has lagged behind our success in other fields. A further breakdown of the accidental deaths, corrected for population changes, for the same two periods reveals a considerable increase in deaths due to accidents of transportation but large decreases in deaths due to poisonings, burns, drownings, firearms, falls and crushings.

Emphasis that these deaths represent only a very small part of the over-all accident picture is given by the admission figures for the Hospital for Sick Children, Toronto, during the five year period 1943-47. Among those children injured seriously enough to be admitted to hospital, the mortality rate was less than 1%.

The two phases of the educational campaign just described are relatively easy to carry out. They involve only the publication of articles by magazines, newspapers, and medical journals at intervals frequent enough to keep the subject constantly before the public eye. The third, and very important, phase is much more difficult to accomplish. Even physicians who realize the need for educating parents in the prevention of accidents find it difficult to blend education on this subject into their busy practices. Even if they do find time for a few words on the subject during an office visit, the anxious mother is apt to forget. Some physicians have mimeographed sheets of safety rules which undoubtedly serve a useful purpose. The best way of filling this vacuum for the majority, however, would seem to be a comprehensive booklet on accidents in children which would be avail-

able to all physicians for distribution to their patients. If such a booklet were available so that the physician could give a copy to each patient it would solve the dilemma of the conscientious physician who cannot find time to do more than urge the mother to read the booklet. At the same time it would help to solve the mother's problem since she would have at hand reliable information on how she could protect her own child against injury or death and, since this information would come from her own physician, its importance would be emphasized.

At the present time the Health League of Canada is endeavouring to have such a booklet printed and made available to physicians either free or at very low cost, for distribution to their own patients. Unfortunately it is not known at the present time whether this will be financially possible. Because of the great value of such a booklet to parents and children alike, it is to be hoped that it will succeed.

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PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

MYRON E. WEGMAN, M.D., *Contributing Editor*

FLUORIDATION OF PUBLIC WATER SUPPLIES

SINCE the first demonstration of a relationship between fluorine and dental caries intensive studies have been carried on by various dental groups, the Public Health Service, and several State Health Departments, looking toward practical application for the general public. Topical application of fluoride has become increasingly popular but even more interest has centered on the possibility of fluoridation of public water supplies.

On November 29, 1951 the National Research Council, Division of Medical Sciences, made public a report of its *ad hoc* Committee on the Fuoridation of Public Water Supplies. This report is worthy of careful study and some pertinent sections are reproduced below.

FLUORINE AND NUTRITION

"1. Under normal conditions of living, fluorine is a trace element in human nutrition. Minute amounts are absorbed from certain foods and drinking water and, to a limited extent, are retained by dental and osseous tissues. The quantity of fluorine ingested in food is a relatively unimportant variable; the average diet contains 0.2 to 0.3 mg. daily. Of greater import is the variable quantity ingested in drinking water. Many of the public water supplies in the United States, particularly those of the large cities, derived from rivers, lakes and ponds, are practically fluoride-free; others contain from traces to 1.5 p.p.m. fluorine or fluorides. A number of supplies (Hill and others, 1949), particularly those obtained from deep wells and aquifers irregularly distributed in various parts of the country, contain from 1.5 p.p.m. up to 7 or 8 p.p.m., very rarely more.

RELATIONSHIP TO DENTAL CARIES

"2. From the epidemiological investigations of Dean (1946), there is convincing evidence that within certain limits there is an inverse relationship between the natural fluoride content of drinking water and the frequency of dental caries in children dependent upon these supplies. The most useful index of the amount of caries is the number of decayed, missing and filled permanent teeth (DMF) per child, per 100 children, or per 100 permanent teeth, at specified ages. . . . The prevalence of caries (DMF) was greatest in those children who had used continuously from birth the public water supplies which were fluoride-free. The prevalence was progressively less in comparable children reared in cities with public water supplies having a fluoride content up to approximately 1 p.p.m. Beyond this concentration there was little, if any, advantage. Children reared in cities where drinking water contained approximately 1.0 p.p.m. of fluorine experienced only about one third as much dental caries as those reared in cities whose water supplies were fluorine-free. . . .

"3. The caries-preventive effect of adequate fluoride intake is principally conferred upon children when the dentine and enamel of the permanent dentition are being formed, i.e., from birth up to about the twelfth year. There is evidence that this increased

resistance to dental caries is carried over to some extent into later life, so that at least there is a delay of several years in the incidence of caries. A recent detailed epidemiological study of adult populations . . . shows that marked caries-inhibitory effects of fluoride waters are operative in the 35-39- and 40-44-year-old groups.

"4. A considerable number of experimental studies . . . in rats and hamsters . . . give consistent support to the concept of a relationship between human caries and fluorides. . . .

Safety Levels

"5. The margin between the optimal quantity of fluoride in drinking water which is required for maximal benefit in tooth development and the amount which produces undesirable physiological effects is sufficiently wide to cause no concern. . . . At approximately 1.0 p.p.m., less than 10 per cent of children show the least detectable evidence of disturbances in enamel formation, which are not visible except to the trained eye of the examining dentist. Beginning at about 2 p.p.m., an increasing proportion of children have mottled enamel of a grade that is easily apparent. While such teeth are caries-resistant, they are esthetically objectionable.

"6. While the safe level of fluoride concentration to afford a maximum caries-preventive effect without mottled enamel is approximately 1.0 p.p.m., it varies somewhat with climatic and other factors and must be ascertained for each general area. For practical public health purposes it has been proposed that a safe level has been reached when not more than 10 to 15 per cent of children age 12-14 years, who have used water supplies since birth, and who have been examined under standard conditions, show the mildest detectable type of mottled enamel. Under the climatological conditions prevailing in the Chicago area, where the mean annual temperature is about 49°F, this upper limit has been reached by domestic water supplies containing approximately 1.0 to 1.5 p.p.m. fluoride. On the other hand, in the vicinity of Moultrie or Brunswick, Georgia, with a mean annual temperature of 68°F, the upper level has been found to be associated with water supplies containing only 0.5 to 0.7 p.p.m.

"7. . . . In accumulated experience there is no evidence that the prolonged ingestion of drinking water with a mean concentration of fluorides below the level causing mottled enamel would have adverse physiological effects. Since the water supplies in various parts of the country contain considerably greater amounts, it is desirable that epidemiologic surveys of the incidence of chronic fluorosis be made in those regions, and that further balance studies be undertaken in order to establish the facts in regard to the storage of fluoride at moderately elevated levels of intake.

Caries Studies with Fluorine in Public Water Supplies

"8. In 1945, studies were begun to ascertain whether the adjustment of the fluoride content of a public water supply to the optimal level with commercially available fluorides would confer the same caries-inhibitory effects as do waters which carry the same concentrations of fluoride naturally.

"Preliminary analysis of the first four years is now available on two studies in which the observations were carefully controlled: (1) the Grand Rapids, Muskegon, Aurora study (Dean and others, 1950); (2) the Newburgh, Kingston study (Ast and others, 1950-51).

Grand Rapids—Muskegon—Aurora Study

"Beginning in January, 1945, sodium fluoride was added to the Grand Rapids water supply in sufficient quantities to insure continuous maintenance of a level of about 1 p.p.m. In order to establish a base line of dental caries experience prior to fluoridation, 19,680 children with history of continuous residence in Grand Rapids, Michigan, were given a complete dental examination. In addition, 4,291 children were examined in Muskegon, Michigan, a city which derives its fluoride-free water supply from the same source as does Grand Rapids, i.e., from Lake Michigan. An additional 5,116 children were examined in Aurora, Illinois, where the community water has contained 1.2 p.p.m. of "natural fluoride" for years. . . . In Grand Rapids, there has been a reduction in caries experience . . . at ages 6, 9, 13 and 16 years, . . . approximately 51 per cent, 36 per cent, 17 and 12 per cent, respectively. Concurrently, there has been a slight decline in the caries rates reported by Muskegon with its fluoride-free water supply but it is relatively small and inconsistent, 22 per cent in the six-year-olds and 28 per cent in the seven-year-olds. This is unexplained. In the 5-, 6- and 7-year old groups at Grand Rapids the DMF rates now approximate those of comparable groups of children in Aurora. Preliminary analyses of the 1950 dental examinations at Muskegon and Grand Rapids indicate that the observed dental caries experience at Muskegon is again similar to that recorded in the 1944-45 base line. At Grand Rapids, a further reduction in dental caries prevalence was observed.

Newburgh-Kingston Study

"In another study, beginning in May, 1945, sodium fluoride was added to the water supply of Newburgh, New York, so as to provide a content of 1.2 p.p.m., while the Kingston, New York, supply was, and has continued to be, fluorine free. . . . In brief, the investigators conclude that the DMF rates among permanent teeth of the 6- to 12-year-old children in Newburgh show a consistent downward trend after four years of fluoridation, whereas the DMF rates in the control city of Kingston show no changes. The reduction in Newburgh is from 20.6 DMF per 100 permanent teeth to 13.9, or a reduction of 32.5 per cent. The rate in Kingston remained at 20.2 DMF per 100 permanent teeth. Since the first permanent molars are the teeth most affected by dental caries, a special analysis of the condition of these teeth was made. The number of caries-free first permanent molars increased in Newburgh, after four years of fluoride exposure among 6- to 9-year-old children, from 59 per 100 molars to 77. The number of caries-free permanent teeth among Kingston children of the same age remained essentially unchanged.

Other Corroborating Studies

"From these two studies, therefore, it appears that the adjustment of the fluoride concentration to optimal amounts in a water supply previously deficient in this element has resulted in considerable reduction of caries in children. Just how great a reduction may be affected ultimately will have to wait upon a longer period of observation. . . .

Choice of Compound

"9. In the control studies to which reference was made in the preceding paragraph, sodium fluoride (NaF) was added to the water supplies. Assuming that the availability

of fluoride ion is the same, the use of sodium silicofluoride (fluosilicate) (Na_2 SiF_6) should result in considerable savings. On the basis of experimental studies, the fluorine in sodium fluoride and sodium fluosilicate produce similar physiological effects upon rats and are equally effective in inhibiting the development of induced dental caries in rats. Accordingly, it is inferred that this would apply to human experience as well, although this has not yet been demonstrated. Other considerations being equal, for reasons of economy the cheaper material (fluosilicate) is recommended. In the case of smaller public water supplies, however, other factors, such as available space, handling hazards, and equipment preference, will determine the choice of the compound used.

Other Factors Affecting Prevalence of Caries

"10. The statement that fluoridation of water supplies reduces tooth decay 65 per cent is postulated on an expectancy for a population using a fluoride-free water supply. When a public water supply naturally containing 0.4 to 0.5 p.p.m., of fluoride is adjusted to the optimal level (1.0 p.p.m.), the reduction in dental caries prevalence obviously would be less. Upon the basis of information at present available, it is not possible to predict how much reduction of caries will be apparent in the adult population. *Other factors—genetic, dietary, bacteriologic, and the availability of dental services, etc.—affect the prevalence of caries and vary in every community. Fluoridation is a partial caries control procedure and does not eliminate the need for other dental health measures.*

Supervision, Surveys and Controls

"11. The promotion, initiation, supervision, and proper operation of the fluoridation of public water supplies is a responsibility of the state department of health, acting jointly through its bureau or division of dental health and through the division of public health engineering with the collaboration of the dental and medical professions. Suitable local plans for dental health surveys before fluoridation and periodic evaluations should be set up by the dental public health program director. These surveys should provide data suitable for calculating an index of caries attack and an index of the frequency and severity of dental fluorosis (mottled enamel). Engineering aspects of fluoridation, such as tests to determine the fluoride content of the water, safety provisions, training of operators, etc., should be covered by state regulations. The statement of policy and procedure formulated by the American Water Works Association (1949) will be acceptable to most state departments of health. . . .

Conclusions

". . . In view of these considerations, your Committee recommends that any community which includes a child population of sufficient size, and which obtains its water supply from sources which are free from or are extremely low in fluorides, should consider the practicability and economic feasibility of adjusting the concentration to optimal levels. This adjustment should be in accord with climatic factors and a constant chemical control should be maintained. With proper safeguards, this procedure appears to be harmless. However, it should be conducted under expert dental and engineering supervision by the state board of health. It should not be undertaken unless this can be provided. How much reduction in the prevalence of caries will actually be realized in a particular community will vary according to local conditions. The procedure will supplement but not supplant

other dental health measures. About one half of the population of this country is living in small villages and rural areas and will not benefit by fluoridation of public water supplies. Other provisions for preventing dental caries in this fraction of the population should be continued and developed."

Support of the policy of fluoridation has come officially from the U. S. Public Health Service, the Association of State and Territorial Health Officers, the American Public Health Association, the American Dental Association and more recently the American Medical Association. It is to the distinct credit of the dental profession and both national and local dental societies that they have been in the forefront of local community efforts to further a preventive technique which should have the effect of reducing the amount of reparative dentistry needed.

Action of New York State Health Department

The New York State Department of Health on January 2, 1952, adopted the following official policy: "The fluoridation of public water supplies is recommended, subject to the provision of adequate control measures in accordance with specified requirements of the State Commissioner of Health. . . ."

The "Requirements for Water Fluoridation Practice" promulgated at the time the official policy was approved covers details of application for permit and review of the equipment proposed to be used. Accuracy of amount of fluoride added is specifically required, since an excess may produce mottled enamel. The maximum concentration is specified at not exceeding 1.5 parts per million at any time. Samples of the water must be taken at frequent intervals for analysis in approved laboratories. Records of amounts of fluorine compound used and of results of analyses must be kept daily. Extensive precautions including toxic dust respirators and use of rubber gloves are prescribed to protect operators of the fluoridation equipment.

Future Extension

It seems very likely, with the amount of endorsement and support that this technique has acquired, that many communities will adopt it. Partial prevention of dental caries is eminently worthwhile but two other aspects should be considered—first, the program must be planned in close cooperation with the state health department and under careful technical supervision and, secondly, other important phases of the community dental hygiene program must not be allowed to languish. In view of the manifest interest in public welfare and community health on the part of the dental profession and the dental societies one may look forward to substantial progress with this new tool.

NEWS AND ANNOUNCEMENTS

Pediatric Postgraduate Course, Burnham Memorial Hospital for Children, Massachusetts General Hospital, Boston, June 9 through June 21, 1952. Daily from 9:00 A.M. to 4:30 P.M. under the auspices of the Harvard Medical School.

Clinics providing a broad review of pediatrics emphasizing the new advances will be given by selected authorities from the Children's Medical, Endocrine, Cardiac, Neuro-Surgical, Thoracic Surgical, General Surgical, Orthopedic, Allergy, Child Psychiatry, Tumor and Rheumatic Services of the Massachusetts General Hospital, from the Ophthalmological and Otolaryngological Services of the Massachusetts Eye and Ear Infirmary and from the Children's Medical Center, Boston.

For further information write: Assistant Dean, Courses for Graduates, Harvard Medical School, 25 Shattuck St., Boston.

* * *

Dr. Katharine Dodd has been appointed Professor and Head of the Pediatric Department at the University of Arkansas School of Medicine. Dr. Dodd was formerly Associate Professor of Pediatrics at the University of Cincinnati.

* * *

Dr. Andrew L. Chute, Toronto, has been appointed professor of pediatrics and head of the pediatrics department at the University of Toronto Faculty of Medicine, Toronto. He will also serve as physician-in-chief of the department of pediatrics at the Hospital for Sick Children.

* * *

A postgraduate conference for pediatricians will be held on June 5, 6 and 7 at St. Christopher's Hospital for Children, Philadelphia, under the sponsorship of the Department of Pediatrics of Temple University School of Medicine. The program will include round table and informal discussions of current problems of clinical interest to pediatricians. Enrollment is limited. Registration fee of $15.00, which includes 3 lunches at the hospital and dinner on June 6th, should be sent in advance to Miss Ruth Portner.

* * *

The following diplomates were certified by the American Board of Pediatrics, Inc.:

ST. LOUIS—MARCH 21, 22 and 23, 1952

Bash, Wallace E., 111 Esmond St., Ft. Wayne, Ind.
Beard, Alice H. Gamble, 7008 Rockwood Road, Little Rock, Ark.
Beck, Karl Henry, 8127 Currie Ave., Wauwatosa, Wis.
Behrer, M. Remsen, 500 S. Kingshighway, St. Louis
Bradlow, Paul A., Capt., MC, Mental Hygiene Clinic, 2128-1 U.S. Army Hosp., Ft. Knox, Ky.
Brigham, Dwight Peter Bent, University Hospital, Omaha
Burnett, John Daniel, 354 Islington Ave., Toledo
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Wheeler, Robert Channing, Suite 414, 636 Church St., Evanston, Ill.
Williams, Hugh Roberts, S. A. Surgeon (R), Division of Epidemiology, Georgia Dpt. of Pub. Health, 1 Hunter St., Atlanta, Ga.
Young, Theodore Everette, R.R. #1, Oxford, Kan.

The Board announces the following date for oral examinations: San Francisco, June 27, 28 and 29, 1952.

BOOK REVIEWS

ANGIOCARDIOGRAPHY, Charles T. Dotter and Israel Steinberg, New York, Paul B. Hoeber, Inc., 1951, 295 pp., $16.00.

This is Volume XX of a series of atlases entitled Annals of Roentgenology, and is the first comprehensive consideration of angiocardiography in a monograph. It is comprehensive and includes discussion of all roentgenologic and clinical aspects of the technic. It is profusely illustrated with reproductions of x-rays and explanatory line drawings of superior quality.

Chapters II and III deal with angiocardiographic and roentgenologic equipment and technic and details the variety of equipment available, although the authors believe that multiple or bi-plane exposures are not necessary for usual diagnostic procedures. Chapter IV must be considered one of the most important in the book and one with which all clinicians recommending the procedure should be familiar. This is a discussion of contrast substances and angiocardiographic mortality, and the authors state that "The principal use of angiocardiography in the child with congenital heart disease is in its demonstration to the surgeon of the abnormal anatomy present. If collateral methods of investigation suffice to rule out surgery as a possible therapeutic approach to any given case, angiocardiography should probably not be performed."

Although syphilitic aortic disease, rheumatic heart disease and other forms of acquired heart disease, pulmonary disease and mediastinal tumors are considered in detail, the major interest in relation to children lies in the chapters devoted to the normal angiocardiogram and noncyanotic and cyanotic congenital heart disease. These chapters, as do others, uniquely blend anatomy, roentgenology, and the physiology of the circulation into a concrete exposition of clinical problems. Minor as well as major aspects of congenital circulatory abnormalities are considered, and the angiocardiographer will find the material presented with excellent illustrations and thoughtful discussion. Careful distinction is made between what angiocardiography can do and what it cannot do, and its usefulness in different circumstances is carefully and critically evaluated.

The book is beautifully edited and published. It becomes at once the indispensable reference to angiocardiographic technic and interpretation.

TUBERKULOSE IM KINDESALTER (TUBERCULOSIS IN CHILDHOOD), Prof. Dr. O. Görgényi, Göttche, Vienna, Springer-Verlag OHG, 1951, 338 pp., 274 illustrations.

In many European countries, the investigation, diagnosis and treatment of tuberculosis has early developed into a specialty. Two factors are responsible for this historical trend. 1: The influence of pioneer discoveries on theory and practice (Koch, Roentgen, Flügge, Ghon, Fahraeus). 2: The increase of tuberculosis in 2 after-war periods of starvation that enabled specialists in well-equipped sanitariums to collect long period observations, to study localisations and differential diagnosis, reinfection and insidious onset, to improve the technic of serial films and to eliminate traditional diagnostic errors. Of particular value is the casuistic material of this textbook, highly instructive in the sections on the gradual development of intrabronchial obstructive lesions and epituberculosis.

Twenty-six chapters discuss all aspects and any pediatrician who knows the German language will find detailed information in any specific question. The chapters are more distinctly separated than in many other European textbooks on tuberculosis, and confusing controversies as well as repetitions are avoided.

Of special interest are the author's personal experiences in the roentgenographic technic of infants (films in sitting position, so-called "Göttche saddle") and the diagnostic errors of miliary tuberculosis. Nontuberculous pulmonary infections (histoplasmosis, etc.) are well presented. Controversial problems (indication, dosage and duration of streptomycin treatment, BCG vaccination) are objectively discussed, and the often opposing views of bacteriologists and clinicians properly evaluated.

The American literature has been thoroughly considered. The bibliography skilfully selects monographs and papers that are fundamental sources of information.

REPORT ON REGIONAL CONFERENCES OF PEDIATRIC EDUCATORS

COMMITTEE FOR THE IMPROVEMENT
OF CHILD HEALTH

AMERICAN ACADEMY OF PEDIATRICS

INTRODUCTION

THE continuing improvement of child health is primarily dependent upon bringing to all children, whether in the city or the country, whether rich or poor, the skillful care of the well-trained physician. This principle has appeared to us self-evident. It is the principle which prompted us, when the Academy's Study was drawing to a close, to seek ways and means for the strengthening of pediatric education. It is the same principle which, more recently, has resulted in a series of informal regional meetings for the purpose of discussing pediatric education and the steps that might be taken toward its improvement.

One of the outstanding findings of the Study is the wide variation among pediatric departments in respect to staff, curriculum, teaching facilities, methods and budget. It is generally agreed that there should be no attempt to press pediatric education into a mold which all schools should then adopt. Freedom to experiment in teaching is as essential to progress in this field as in the field of laboratory research. Nevertheless, a certain element of standardization was almost inevitable as a result of the procedures used for scoring. The levels which were expressed as optimal then assumed the nature of standards. Individual department heads have shown considerable interest in the relative positions of their departments as established by the scoring and, in respect to those aspects in which the departments stood comparatively low, effective use has been made of the data in the direction of the optimum levels established for the scoring. Furthermore, during the Study and subsequently, many department heads have requested an opportunity to meet together for the sole purpose of talking over their problems in pediatric education rather than, as is usually the case, for the purpose of reading and reviewing scientific papers.

For these reasons the Committee for the Improvement of Child Health sponsored the series of meetings which have been summarized in the following pages. These meetings were organized on an arbitrarily selected regional basis. An attempt was made to bring together those who have similar problems from a geographic point of view and at the same time to keep the gatherings small enough for free and informal discussion. Also, since pediatric education is a function which concerns the Academy at national, district and state levels, the district and state chairmen participated in the meetings in the areas where there are medical schools. Between October, 1949, and May, 1950, such meetings were held in Detroit, San Francisco, New York City, Philadelphia, Winston-Salem, Kansas City and New Orleans. The one member of the Committee's staff who was able to attend all of these meetings was Dr. Glidden L. Brooks, to whom we wish to express our gratitude for recording the meetings and preparing the following summary.

WARREN R. SISSON, M.D.
JOHN P. HUBBARD, M.D.

REPORT ON REGIONAL CONFERENCES OF PEDIATRIC EDUCATORS

Function of a Medical School Department of Pediatrics

THE basic functions and organizations of a department of pediatrics in a medical school were widely discussed, although a comprehensive definition was not attempted. It seemed clear that, at the undergraduate level, the function of the department is to introduce the student to pediatrics. This implies the immediate objectives of (1) teaching the student to care for sick children; (2) teaching him an approach to the child as a part of the human community; (3) acquainting him with the nature of the practice of pediatrics, (4) demonstrating the significance of physical, mental, and emotional growth and development of the child; and (5) making him aware of the research discipline as it applies to the health problems of children. Equipped with such an introduction, the student should then be able to enter general practice, pediatrics, or any of the medical specialties, with a fundamental appreciation of and approach to the pediatric problems which he may then encounter.

In addition to this basic function there are, of course, many other responsibilities which must be undertaken by a department, depending upon the circumstances under which it may be operated. These include such activities as research, community service, training of pediatricians, postgraduate education and the like. Each of these, of course, has a more or less indirect bearing on the nature and quality of undergraduate instruction.

Detailed discussion at this series of meetings was concerned with the organization and methods necessary to accomplishing these broad objectives with primary attention to undergraduate teaching. Since these sessions were of an exploratory nature, they were conducted as informal round table discussions and, outside of a few suggested considerations, no limitations were set either as to subject matter or methods of approach. Each meeting was allowed to follow the thoughts and inclinations of those attending so that a broad pattern or basis for future activity might unfold.

Several of the meetings drew attention to the current shift away from disease to health supervision of the well child and from in-patient to out-patient teaching. As the nature of pediatric practice alters, parallel changes must take place in pediatric teaching. Pertinent to this was the discussion at one meeting of the need for constant re-examination of the major objectives of a pediatric department so that stock may be taken as to whether departmental organization, staff and techniques are best adapted to accomplish these objectives.

Evaluation Schedule or Score Sheet

The score sheet used in the Study of Pediatric Education provided a useful point of reference for discussion since it naturally introduced a number of basic considerations pertinent to the activities of all pediatric departments represented. It was the consensus that a method for continuing evaluation and relative ranking of departments of pediatrics in medical schools was desirable for several reasons. The value of periodic evaluation as a stimulus and guide to improvement is obvious. Soon after the completion of the Study, a copy of the completed score sheet for each department together with information as to

the relative rank of that department was sent to the chief of pediatrics at each medical school. This information has been used effectively in several instances with deans and other administrative officers to demonstrate the necessity of meeting certain needs within the pediatric department. Since the Study, a number of schools have reported impressive improvements and at least two have more than doubled their previous rating.

The development of a continuous schedule of evaluation entails certain practical considerations. Because of necessary limitations of expense and personnel it is not feasible to establish a system of periodic visits to pediatric departments, after the pattern of the original Study. Therefore, the system must be devised for self-evaluation, supplemented by correlation for ranking and informational purposes at a central office. Since, as will be seen later, there is not yet unanimity in respect to many items used in scoring, any evaluation schedule must be fluid and subject to constant revision, addition and subtraction. Admittedly such an undertaking is difficult but there are already valuable precedents now being applied in the field of medicine. Examples are the recently developed hospital rating sheet of the American College of Surgeons and the evaluation schedule for local health practices of the American Public Health Association. It should be observed that both of these have evolved after years of experimentation.

A revision of the Study score sheet adapted for self-evaluation purposes has been prepared, utilizing the suggestions emerging at these meetings. It is recognized that, initially, there may be both gaps and injustices which detract from its usefulness; it will require frequent change of emphasis since the nature of pediatrics itself is not static. Nevertheless, it is hoped that from it will evolve a useful administrative and pedagogical tool.

Organization of a Medical School Department of Pediatrics

An item pointing out the desirability of having pediatrics accorded full department status within the medical school has been included in the schedule. At the present time almost all schools have pediatrics set up as a separate department. It was felt, however, that the principle concerned was of sufficient importance to warrant its retention in the evaluation scheme. In one school the final separation of pediatrics as an autonomous department came about as a direct result of the Study of Pediatric Education. At the same time, it was pointed out that there is in some schools an increasing tendency to break down departmental barriers in favor of horizontally integrated teaching. This evaluation sheet item does not imply disapproval of such a practice but simply implies that pediatrics should occupy the same organizational status as other disciplines of comparable importance in the medical school curriculum. Thus, for example, the professor of pediatrics should exercise the same prerogatives as the professor of internal medicine in seeking his department's share of the medical school budget or curriculum hours.

Staff

The discussion of the relative importance of full-time and part-time teaching was lively and pertinent at several of the meetings. There was no argument over the desirability of leavening so-called "full-time" teaching with precepts and experiences derived from teachers whose main activity is the practice of pediatrics. The mooted question was which type of teacher should head the department. Though by no means unanimous, the consensus affirmed the principle that effective administration and leadership of a university department of pediatrics requires the talents of a person whose major activity and re-

sponsibility lies within the school. At the same time it was recognized that exceptions might (and indeed do) exist in which a department gains in efficiency and support by having at its head one who also engages in pediatric practice in the community. It was also agreed that where a part-time teacher acts as department head it is very necessary that he have one or more full-time members of the department.

Inevitably, discussion on this point brought up the need for a definition of what is meant by "full-time." Although no altogether satisfactory definition has emerged, it is generally agreed that to be classed as "full-time," a man must devote the bulk of his time and responsibility to departmental activities (teaching, administration or research) and that any other activities must be such as not to interfere with his major duties. It is conceded that it is permissible and indeed desirable for a full-time man to see private patients in consultation since this relationship does not imply a "doctor-patient" responsibility in its usual sense. As a result of the discussions, full credit in the revised evaluation sheet has been retained for a full-time department head but additional credit is given for full-time staff members regardless of the status of the department head. Also, since the basic function of any medical school is to teach medical students, it must be recognized that the primary value of any staff member, be he full or part-time, lies in the amount and character of his contact with students. Therefore, attention must be paid to whether or not staff members actually engage in teaching.

Objective measurement of quality within a department is in any complete sense impossible in any self-evaluation schedule. This type of measurement can be done effectively only through a series of visits by a competent and qualified observer such as was done at the time of the Study. It is noteworthy that when the schools were rated according to the qualitative observations made by Dr. John Mitchell after he had visited each medical school, this list showed a high degree of correlation with the rank as established by the score sheet. Just as the quality and "tone" of a department is only imperfectly measured by an evaluation schedule, so likewise is an assessment of the qualifications of the individual teachers within the department. Fortunately, however, in the pediatric field there exists a competent certifying body, the American Board of Pediatrics. Furthermore, some evidence of the general interest and acceptance of a man within the field of pediatrics can be gained by the fact that he is a member of one of the several recognized national pediatric groups. It was therefore generally agreed that a high percentage of staff, either certified by the American Board of Pediatrics or having membership in the American Pediatric Society, the Society for Pediatric Research or the American Academy of Pediatrics, provides an additional measure of general staff quality. On several occasions it was pointed out that members of a pediatric department staff may be thoroughly accredited in an allied field such as, for example, psychiatry or pathology; therefore, it was advised that this item be modified in the revised score sheet to include credit to cover the qualifications of staff members properly certified in allied specialties.

It is generally recognized that the character and teaching potential of any medical school department is distinctly enhanced by the inclusion of the research discipline in its activities. It was also pointed out that those who are conducting research also do a good deal of teaching and hence add to the department's teaching potential. Even an isolated research unit, in which the workers have no contact with the students, may raise the general level of excellence of the department and indirectly influence the attitudes imparted to the students.

Clinical Facilities for Teaching

Since pediatrics is primarily a clinical subject, the basic facilities essential to a pediatric department are those which are also used for the hospital and out-patient care of children. In many respects it is extremely difficult for the quality of teaching in a medical school department of pediatrics to transcend the limitations placed upon it by the teaching hospital and out-patient facilities controlled by the medical school. The number and excellence of such facilities available to departments of pediatrics was found in the Study to show the same wide variation that was evident in other aspects. Here again it is difficult to assess the quality of hospital services. One factor of obvious importance is whether or not the pediatric service used for teaching medical students is also approved for training of pediatric residents. In the American medical school system, the experiences in the clinical undergraduate years are continuous and interdependent with the clinical experiences in the interne and resident phase of medical training. Any hospital service which is unable to meet the rather fundamental requirements for approved residency training in pediatrics must likewise be seriously handicapped in its capacity to provide a proper clinical atmosphere for medical students. A good part of a young doctor's training is received from those immediately preceding him in this student-interne-resident hierarchy. This training is either deficient or entirely lacking in a hospital which cannot attract residents by virtue of having an approved position.

The number and variety of patients available for teaching purposes is a basic factor affecting both the character and completeness of pediatric undergraduate teaching. Generally speaking, the greater the number of patients available for teaching purposes, the wider the variety from which material for students may be selected, both in respect to pathological conditions and problems of well children. On the other hand, the total patient load in relation to staff and students must not be so great that all of the energies of both groups must be occupied with the purely service aspects of caring for a vast number of patients and allowing no time for effective teaching, research and reflection. There is, of course, no maximum limit as to the size of clinical facilities in a teaching hospital. Limitations imposed by largeness have to do largely with the ratio of staff to patient load. On the other hand, a hospital can be too small to carry the teaching load and may need to be augmented in order to obtain the necessary number and variety of patients for instructional use. In general it was felt that during his pediatric training a student should see between 15 and 20 new in-patients and a comparable number of out-patients. In addition to those patients actually assigned to the student during his clinical clerkship, there should also be sufficient variety of patients available to illustrate various categories of pediatric interest.

Direct control of the use and occupancy of clinical facilities for teaching on the part of the department of pediatrics is desirable and is thought by some to be essential to effective organization for teaching. On the other hand, it is recognized that in many instances it is necessary to supplement teaching by use of beds which are not necessarily under administrative control of the department itself. Paramount to the effective use of such beds, however, is what is termed supervisory control. By this it is meant that the department or its staff members have full responsibility for the *medical care* of the patients occupying these facilities although formal administrative control may lie elsewhere. All teaching for which a pediatric department assumes credit or responsibility should be done by an individual holding an appointment in that department, a member,

so to speak, of the departmental family. If this is not so and students are simply farmed out to institutions such as communicable disease hospitals or psychiatric units and are taught by whomever happens to be available in these institutions without regard to establishing departmental relationship, it is obvious that no control of the quality, content, or philosophy of teaching can be effectively exercised by the department of pediatrics.

Budget and Financial Problems

The accumulation of budgetary data and its statistical analysis were found to be extremely difficult because of the wide variation in accounting practices among medical schools. It was the consensus that for future self-evaluation purposes such data, for the school as a whole and the share allocated to pediatrics, while interesting, did not justify the difficulties in obtaining it in a usable form. It was agreed that the basic consideration which confronts the pediatric department head and which bears upon the quality of pediatric training in a medical school is the budget of the pediatric department itself and its relation to the number of students taught. In order that comparisons between pediatric departments of different schools could be effective, the following divisions of the budget were defined. The Basic Budget of a department of pediatrics includes money accruing to the department from the medical school, endowments, hospitals, and other sources on a continuing basis. This Basic Budget, then, represents funds directly available for teaching and maintenance of the department. The term Supplementary Budget is used to describe funds which accrue to the pediatric department for special purposes, such as research grants for categorical projects or endowment funds for research institutes, the personnel of which may be available for teaching but whose primary function does not pertain directly to the pedagogical function of the department. It was the consensus that the basic budgetary funds were those of prime importance and the most credit should be allotted to such a budget in any evaluation. At the same time, the necessity and advantage of having supplementary funds to support research within the department is recognized in the revised score sheet and departments continue to be rated on their total budgetary resources.

The universal problem of trying to obtain sufficient funds effectively to operate a department of pediatrics was found to be common to all participants in these conferences. Possible sources of additional funds were discussed. In the case of two of the departments represented, departmental revenue is obtained through the organization of the medical school and hospital on a pay clinic basis. In these schools, all or at least the key department personnel are full-time members of the hospital staff and medical school faculty. Their services, consultative or otherwise, in the care of patients within the hospital are billed to the patient by the medical school and the income received therefrom utilized to finance the entire medical school and allocated to departments on an equitable basis. At the meetings where this system was described it was the consensus that the plan had great merit and perhaps represented the only solution to the continued financing of medical schools by private funds. It was felt, however, that the limit of income earned for the medical school by any departmental staff should not be set by the school at any minimum figure which would force the staff to divert their energies away from pedagogical responsibilities toward the service demands of the situation; that insofar as was economically possible, all staff members should be given complete freedom in the number of consultations or patients seen. In the ideal department so organized, certain staff members would have little or no consultative or service function but would concentrate

entirely on teaching and research, while other staff members might devote the bulk of their energies in the service category, thus assuring the department of an adequate income without compromising the time available for teaching.

Federal Aid

The problem of whether or not Federal subsidy of pediatric education was necessary or desirable was discussed at length. It was the consensus that if private funds were available they were preferable to funds from governmental sources, but that failing this, Federal support of departmental activities should be accepted and sought after. The necessity for keeping these funds free of political or unnecessary bureaucratic control was repeatedly emphasized. It was also pointed out that the support and sympathetic understanding of the entire pediatric group was essential in obtaining funds free of control from either private or Federal sources. The need for a more sympathetic understanding of the financial problems of pediatric education on the part of the practicing pediatrician might be met by the continuing interest of the American Academy of Pediatrics in this problem. The presence of Academy representatives from outside the educational field of pediatrics was felt to be desirable at these meetings and it was agreed that an attempt should be made to continue this representation in future discussions.

Among the financial needs repeatedly mentioned was that of obtaining funds in order to pay the part-time clinical teacher for the time spent in medical school activities. Due credit was given to accomplishments of the voluntary system of part-time teaching as it has existed in the past and now exists, but it was pointed out that the increasing demands of practice and the necessities of the present economic situation make voluntary teaching increasingly difficult. This is especially true among the younger pediatricians, from whom future teachers must be recruited. Another recognized financial need is that of providing funds to a department for the purpose of training teachers of pediatrics. In the past such teachers have been supported by grants for categorical research during their post-internship training period. The uncertainties and inequalities of this method of finance make the desirability of recognizing this need urgent.

Content of the Pediatric Course

Before a detailed consideration of curricular content in a medical school course in pediatrics can be undertaken it is necessary to examine carefully the rather basic question of how many actual hours a student should spend during his four years in medical school. As a point of reference it may be assumed that, since pediatrics is a clinical subject, the bulk of pediatric teaching will fall into the so-called clinical years, usually comprising the 3rd and 4th years of a normal 4-year medical course. The total number of curriculum hours available in the last two years of medical school usually lies between 4500 and 4800. How much of this total bloc of curriculum hours should be allotted to pediatrics is the concern of pediatric department heads who must seek time enough to cover the subject adequately, and medical school deans who must equitably budget the hours available among the clinical departments. No one would contend that, because a third of a general practitioner's patient load lies in the pediatric age group, a similar proportion of medical school clinical hours should be allotted to pediatrics. A great deal of the pediatrician's armamentarium is obtained not only from his basic science years but also from his clinical teaching in undergraduate departments of medicine, surgery and allied specialties. During the Study of Pediatric Education it was shown that a number of schools

allot less than 200 curriculum hours to pediatrics, whereas others approach the 500 mark or even exceed it when overtime is taken into account. The median was approximately 300 hours. These facts indicate that there is no general agreement or accepted practice common to the majority of medical schools. In discussing this point, it was quickly agreed that fewer than 300 hours allotted for pediatrics was probably not adequate, but it was also pointed out that an optimum number of hours must exist beyond which additional time spent did not necessarily imply more effective teaching in pediatrics. In other words, it was recognized that over-emphasis on pediatrics to the detriment of other essential clinical subjects not only unbalances the entire school curriculum but may well produce students with an inadequate understanding of essential clinical fields closely allied to the care of children. Within certain limits, effective horizontal integration of teaching within a medical school necessarily cuts down the number of hours officially allotted to any one department. Therefore, in a school which shows an excessive number of hours allotted to pediatrics there is need for careful interdepartmental consideration of what is being taught in each specialty so that wasteful duplication of teaching may be avoided. Parenthetically, it was pointed out that in some instances duplication of teaching is not altogether a bad thing and may be necessary to develop a thorough understanding of certain complicated clinical processes common to children and adults. Considerable time was spent during the meetings in discussion of the problems of proper integration of pediatrics with other departments. Department heads who have recently been concerned with establishing entirely new clinical departments of pediatrics described their experiences illustrating the value of scrutinizing what is being taught by other departments and then establishing at the outset a working agreement with such departments as medicine, surgery and obstetrics in respect to curriculum content bearing on the pediatric age group.

In final summation of the question of total hours, it was the consensus that in any system of evaluation no additional credit should be given for curriculum hours in excess of 400, although it was recognized that the whole question of total hours and horizontal integration should be carefully re-examined at future conferences on pediatric education.

Although pediatrics is taught mostly in the clinical years of medical school, there was lively discussion as to when and how it should be introduced into the medical school curriculum. A sizable number of departments reported that a series of introductory lectures on pediatrics were given during the second year, sometimes integrated with basic sciences being taught at the time and sometimes grouped separately as a formal introduction to pediatrics. In a few instances pediatrics was integrated into the first year curriculum. Although there is a wide variety of approach to the problem of introducing the medical student to pediatrics, the one most commonly agreed upon was to introduce the student first to the factors of growth and development, especially as they concern the normal child. Although a number of interesting techniques for doing this were described, it was generally agreed that the chief problem attending this approach lay in the difficulty of making the subject interesting and understandable to medical students at that stage in their medical education.

There was almost unanimous agreement that the keystone of a medical student's undergraduate pediatric career is the clinical clerkship and that here lies the need for the greatest emphasis and organization. Discussion of clinical clerkship reflected the same increasing appreciation of the paramount value of out-patient versus in-patient training, which has been mentioned heretofore. A true clinical clerkship implies that the student participates in obtaining the history from the parents and in the conduct of the care of the patient on

the ward or in the out-patient department, including some responsibility for basic laboratory data. In a number of departments it is the custom to permit the third or fourth year student on the clinical wards only as an observer. In such a situation, although the student is assigned a patient and follows the course of his diagnosis and treatment, he does not otherwise participate in the medical management of the patient. It was the consensus that a more effective and stimulating teaching device exists where the student's history becomes a part of the hospital record (supplemented of course by notes by the house and visiting staff) and the student directly assists in diagnostic and therapeutic procedures carried out during his patient's hospital visit. Furthermore, the desirability of assigning responsibility for laboratory work to the students outweighs in a well-organized service any danger of exploitation or otherwise wasting the students' time on relatively routine occupations. It must be admitted that this full clinical clerkship occasionally encounters medicolegal questions, may work a hardship on the house staff and the parents and is sometimes productive of rather unreliable laboratory data. These objections are not insurmountable since such clinical clerkships are offered by many medical school departments of pediatrics at the present time. The need for direct departmental control within the teaching hospital, however, is obvious in any such arrangement.

The chief difficulty encountered in adapting this type of clinical clerkship to the out-patient department is usually one of too small a space for teaching and too large a patient load to permit individual instruction on the part of the staff.

In considering the items concerned with out-patient teaching, it was repeatedly emphasized that this phase of medical education is attaining more and more importance as the changing character of pediatric practice is influenced by the use of antibiotics, improved diagnostic methods and increasing attention to the problems of the well child. It has long been the custom to teach third year students in the out-patient department and then graduate them to the supposedly more challenging and complex in-patient problems in their final undergraduate year. Already a number of departments report a reversal of this trend and are attempting to fit their students for more effective practice by concentrating the most experienced group and possibly the most sophisticated teaching in the out-patient department. It is admitted that this is often difficult to achieve due to limitations of space, control of patient load and difficulty in marshalling sufficient instructional force to provide the intimate small group type of teaching which the out-patient requires. The number of department heads and senior staff members who actually perform an effective amount of out-patient teaching is still distinctly a minority. Although the desirability of the principle was generally accepted it was felt that emphasis should not yet be placed on it in the evaluation sheet although such emphasis might well be added in future revisions. Credit, however, continues to be given for a high ratio of instructors to students in the out-patient department.

In both the out-patient and in-patient periods of clinical clerkship, it is desirable that the student be made available to the pediatric hospital service on a full-time basis for a continuous bloc of time, in order that he may properly discharge his responsibilities without interruption. Department heads from all schools where this system was possible expressed the greatest satisfaction with its results.

In addition to the basic pediatric training received by the student on in-patient children's wards and in out-patient department exercises, there are many departmental problems associated with the teaching of special phases of pediatrics. In considering these

special problems from the standpoint of undergraduate education, it is not clear how much emphasis should be placed on them in the medical school and how much should be left for the interneship and residency period of medical education. It was generally agreed that detailed consideration of such areas as care of the newborn, prematures, handicapped children, dental problems and so forth, were best left to the postgraduate years. Nonetheless, it is necessary that a medical student have some appreciation of the nature of these problems, in order that he may grasp the full concept of pediatrics as a division of the medical sciences. The problems relating to these special considerations are rendered more difficult by the fact, as shown in the Study, that a fair percentage of students graduating from medical schools today have little opportunity for effective pediatric training during subsequent interneships, especially those interning outside of a hospital which is approved for pediatric residency training. Therefore, the amount of training obtained in his undergraduate years may be all the training a doctor has in these important aspects of pediatrics at the time he enters practice. Against this need must be balanced the practical considerations of fitting such instruction into an already crowded pediatric curriculum and adapting available facilities for effective student instruction.

There was no argument as to the soundness of the principle that every medical student should have some instruction in the care of the newborn infant. The amount and nature of such instruction was not so readily agreed upon. The chief difficulty encountered in attempting to orient medical students in the care of the newborn appears to be the obstacle presented by modern techniques designed to protect the newborn from exposure to infection. One group felt that this potential danger was of sufficient magnitude that all such teaching takes the form of demonstrations which are observed but not directly participated in by the medical students. The opposite school of thought maintains that this type of instruction affords the student an inadequate introduction to this aspect of pediatrics which may play so prominent a part in his practice in the future. This conviction was especially strong in those departments which share in a medical school policy of training physicians largely for general practice. It was felt that for effective understanding of the problems of newborn infants the student should have an opportunity to participate in the examination and actual care of the newborn infant. It was pointed out that the danger of cross-infection in such teaching, if properly controlled, could be minimized, since the chief danger to the newborn infant lies in contact with other newborns more than in exposure to adults. The importance of both points of view is so great that a thorough consideration of effective techniques of teaching newborn infant care should be subject to further elucidation at future conferences on pediatric education.

Closely allied to the instruction of the medical student in the care of the newborn is the question of his orientation to the problems of prematurity. In a number of schools, prematures are not considered suitable material for undergraduate instruction and all contact with this problem is reserved for the postgraduate years. On the other hand, the need for an appreciation of the premature problem was emphasized at a number of the meetings. Also the value of the premature infant in supplementing the teaching of basic aspects of growth and development was pointed out. It was the consensus that medical students should have at least an introduction to the problems of prematurity during their undergraduate years, but that clinical exercises must necessarily be restricted to demonstrations in physical situations where the student is separated by a mechanical barrier from the premature infant.

A sound understanding of the principles of growth and development, not only from the physiological point of view but also from the point of view of rearing children in our present day social and economic environment, is fundamental to any effective undergraduate instruction. Although time did not permit exhaustive discussion of this problem at any of the meetings, there was frequently expressed a feeling of dissatisfaction and inadequacy at the manner in which this basic part of pediatrics was being taught. It was the feeling of many that more effective integration of this phase of pediatrics into the curriculum was necessary.

While there was general agreement that the above-mentioned facets of the pediatric discipline should be a part of every undergraduate medical school course, there was considerable confusion as to which of the many other special problems of pediatrics were worthy of special emphasis in the undergraduate curriculum. These areas of special training include such important factors as emotional disorders, dental care, speech and hearing defects, cerebral palsy, blindness, epilepsy, institutional problems, adoption and foster care, community services and many others. Obviously, since each meeting was limited to one day and faced with a rather comprehensive agenda, detailed discussion of each of these was impossible. It was agreed, however, that each should be considered and its relative importance assessed, as well as the most effective way of introducing it into the curriculum. The general impression gained from the meetings was that each department head felt a sense of strong conviction that most of these special considerations belonged in the undergraduate curriculum but also felt a sense of frustration as to how each could be effectively taught without compromising another equally important or perhaps more basic aspect of pediatrics.

Techniques in Pediatric Education

The members of the medical profession have a strong heritage and tradition as teachers. Medicine and its various branches have been taught in a self-perpetuating fashion. Thus, teachers of pediatrics today are primarily physicians who have been taught by other physicians and who have taken upon themselves the obligations of becoming educators. With very few exceptions, none of the teachers of pediatrics has any formal training or basic introduction in the field of pedagogy. The question was recurrently raised as to whether or not benefit would accrue from having professional educators from the "teachers' colleges" invited to scrutinize pediatric teaching methods and suggest ways of improving them. In at least three medical schools this has been tried in one form or another. As reported at these meetings, the experience gained from such consultations was uniformly disappointing. A certain amount of the theory of education was transmitted but those who had the experience felt that little of practical value was accomplished. In contrast to the unrewarding results of seeking help in the general aspects of pedagogy, a number of instances were reported where valuable suggestions and aid were obtained from outside sources in solving special problems of teaching techniques. For example, the department of public speaking in one university rendered valuable assistance in improving the content and manner of case presentation and discussion at conferences. Practical teaching methods and guides were also obtained in several instances from personnel department of large industries and from the instructional methods utilized by the Army and Navy training programs.

Considerable interest was expressed in developing audiovisual aids for use in pediatric instruction. The use of motion picture films for teaching was considered desirable but it

was repeatedly pointed out that available films on pediatric subjects leave much to be desired. Also, in the few effective films available, the comments contained on the sound track of the film are frequently not applicable to the points which should be emphasized in teaching medical students. It was suggested that such films might be better utilized by disconnecting the sound track and having the instructor furnish comments as the film is shown. In addition to these disadvantages the expense of producing satisfactory movie films was generally recognized as a deterrent to very wide development of this method in the pediatric field. It was the consensus that as visual aids, still pictures are generally superior to motion picture films. The desirability of establishing a library or loan collection of suitable collections of slides or photographs for teaching aids in various pediatric subjects was frequently emphasized. It is reported that the Society for Pediatric Research is planning to establish such a collection in the near future. At several meetings it was the consensus that the Academy might render a valuable service by establishing a clearinghouse for information as to technical and mechanical aids available for use in pediatric teaching.

An important aspect of the discussion at most of the meetings was a rather strong divergence of opinion in respect to the value of didactic lectures in clinical teaching. Some department heads expressed a strong conviction that such lectures were of no value whatsoever in teaching pediatrics and a few have implemented this conviction by abandoning such teaching entirely. Others disagreed sharply with this point of view and felt that a large number of didactic hours were essential to a proper introduction of the subject of pediatrics. This divergence of opinion is reflected in practice as reported by the various medical schools at the time of the Study of Pediatric Education. In general, it was apparent from the discussion that there is a definite trend away from emphasis on didactic teaching, but that the majority of department heads still favor the retention of introductory and explanatory didactic sessions to supplement individual bedside teaching.

There was general agreement that the keystone of pediatric teaching lay in the techniques having to do with the skillful and effective use of patients as examples of the varied subject matter pertinent to proper introduction of the child to the student. It was indicated, for example, that a child is after all the best illustration of the principles of growth and development, just as a child with pneumonia is the most effective illustration and springboard for a discussion of the pediatric aspects of infection of the pulmonary tree. It was agreed that there was need for a great deal more detailed discussion of this technique of clinical teaching than time permitted at any of these meetings and that, in the future, seminars might well be devoted to one or another aspect of such teaching.

Interest was frequently expressed in the development of techniques for introducing the student to the family and community aspects of pediatric practice. At several schools, in order to accomplish this objective, students are either required or permitted to spend a term of "preceptorship" in the office of a physician. Rather than a strictly pediatric exercise, this is usually a part of the general medical curriculum and the student is assigned to a selected general practitioner, preferably in a rural or small community setting. The need for careful selection and supervision of such preceptors was repeatedly emphasized. In other schools the pediatric service either operates or participates in a domiciliary case service in the city in which the school is located. It was suggested that the addition of a carefully selected general practitioner to the pediatric department staff might be a valuable aid to accomplish this objective. Most such techniques are now in an experimental phase and the need for future consultation in respect to these techniques is evident.

Pediatric Interne and Residency Training

The discussion of pediatric residency training was concerned at several meetings with the need for periodic re-evaluation of hospitals approved for pediatric residency training. It was pointed out that the current system of approval by the American Board of Pediatrics and the American Medical Association Council on Education and Hospitals is cumbersome and makes no provision for changes which might occur within a service after approval. Members of the Board of Pediatrics who were present at these meetings pointed out that the Board is well aware of these problems and is now taking tentative steps for providing inspection of hospitals to supplement that accomplished by the American Medical Association. They also stated that the Board would be very pleased to relinquish its prerogative of approving hospitals for training and simply function in its primary capacity of a certifying board if there could be some other method devised for approval of hospitals for training. At the present time, however, the Board feels obligated to continue to function in this capacity.

The problem of decentralization of pediatric residency training was widely discussed. A number of departments represented have had experience in rotating their residents through community hospitals, thereby effecting a medical school affiliation for the outlying hospitals and providing further clinical experience for their residents. It was the consensus that although there were many difficulties in carrying out such plans, the advantages accruing both to the resident and to the hospitals outweighed the disadvantages. The chief danger lies in the possibility that the outlying hospital may exploit the resident in developing the service function of the hospital at the expense of his educational experience. It was generally agreed that very careful supervision must be provided by the teaching hospital and accepted by the outlying hospitals through which the residents are rotated. Those who were considering inaugurating such plans pointed out that the supply of residents available to hospitals was greatly diminished from the heavy demand for residencies that existed during the first post-war years. A number of department heads were opposed to the principle of decentralization on the basis that a resident applying to a teaching hospital expects to have his entire assignment there and that decentralization represents dilution of his training. The fear was expressed that a hospital which rotates its residence elsewhere, if only for a couple of months, might become unpopular and hence draw on a less desirable applicant for residency. Opposed to this point of view was the criticism that neither medical students nor residents in pediatrics were being effectively fitted for the assumption of community responsibilities which inevitably should become the duty of any practicing pediatrician. Those who held this view felt very strongly that decentralization of training, by placing a resident in a community hospital situation, was of very great value in orienting him toward this practical responsibility of his future career.

In general, the group attending these meetings seemed much more satisfied with the present character and extent of residency training for pediatrics than they were with the opportunities in pediatrics being offered the rotating interne. So far as the house staff is concerned, the service at the usual teaching hospital is oriented toward the pediatric resident rather than toward the interne, who spends only a few months on the pediatric service. A need for more attention to the problems of the rotating interneship is accentuated by the fact that this type of interneship is not only required by law in certain states, but also is becoming increasingly popular with medical students. One university reported that the entire graduating class from medical school the previous year had applied for

rotating interneships and there was not one single applicant from the medical school for a straight service at the university hospital. Related to the problem of the rotating interneship in pediatrics is the question of the pediatric content of the recently established residency for general practice. The discussion on this matter was concerned chiefly with the need for further consideration and little progress was made toward solution of the problem at these preliminary meetings.

There was also discussion of the responsibility of the medical school department of pediatrics for postgraduate training beyond the interne and residency level. At least two department heads expressed the strong conviction that the medical school had no responsibility whatsoever in this direction, but that such instruction was more properly a function of local medical societies, state medical society, and hospital staff. Other department heads did not share this view, but pointed out that in many medical schools responsibility for postgraduate instruction was thrust upon the department and there was no alternative but to accept it. The majority of pediatric departments represented did report provision for postgraduate education in one form or another, although there was wide variation as to the amount of time devoted to this aspect of education. It was generally agreed that even though a pediatric department did not take the responsibility for the conduct of postgraduate courses, it was incumbent upon the department of any medical school to furnish, at least in part, the instructional staff for such courses given in the medical school area.

Role of the American Academy of Pediatrics in the Field of Education

At all of the meetings there was the greatest interest in the future participation of the Academy of Pediatrics in affairs of pediatric education. It was repeatedly urged, and in several meetings stated in formal resolutions, that the Academy should continue an active interest in pediatric education. The reasons for this are several: (1) At the present time the Academy is the only nationwide organization in the field of pediatrics which is so organized as to be able to implement effective action in pediatric education. (2) There is a growing need for closer understanding and cooperation between the practicing pediatrician and the teacher of pediatrics. The problems of the two are closely interrelated and without mutual understanding and sympathy necessary progress is seriously impeded if not rendered impossible. (3) By means of the Study of Pediatric Education the Academy has authoritatively established itself as an active force in this field. (4) In these preliminary meetings on pediatric education the Academy has established a pattern which may prove useful in implementing the programs designed to bring about improvements in areas indicated by the Study of Child Health Services.

It was the consensus that future meetings on pediatric education should be sponsored by the Academy, both on a regional and on a national basis. There was considerable discussion as to how a national one-day meeting of pediatric educators could be fitted into the existing Academy meetings and the prevalent feeling was that such a national meeting might very well be made a part of the annual areal meeting of the Academy. There was also some discussion as to other methods of holding such meetings, but it was felt that recommendations arising at these preliminary meetings should be confined to a request that the Academy consider continuing to sponsor such meetings, which should include not only pediatric educators but also representatives of the practicing pediatrician group and possibly other interested parties.

In order to develop an effective evaluation schedule and maintain a source of information as to comparative accomplishments by schools, a continuing committee must be charged with this responsibility. Periodic observations must be made and agreements reached as to the relative value of individual items in the schedule as well as its over-all usefulness. Experience of others has shown that frequent alterations of emphasis and even complete changes of format usually must be made before an instrument of maximum value is developed.

It appears that, at present, the American Academy of Pediatrics is the only organization so constituted as to lend itself to an undertaking of this sort in the field of pediatric education, and having already made an auspicious beginning, this activity should be continued. This might either be a function within the central office of the Academy or delegated to a committee. Either method entails expenditure for secretarial help, printing, postage and travel for consultative purposes. However, it is felt that this represents a service of distinct value to pediatric education and thus to the whole field of child health.

APPENDIX A

Pediatric Educators and Academy Representatives Attending Series of Meetings on Pediatric Education

Detroit, October 26, 1949

Dr. Paul V. Wooley, Jr., Chairman ..... Wayne University
Dr. James L. Wilson ..... University of Michigan
Dr. Matthew Winters ..... University of Indiana
Dr. Leonard T. Davidson ..... University of Louisville
Dr. Samuel Spector ..... Western Reserve University
Dr. Earl H. Baxter ..... State University of Ohio
Dr. Warren E. Wheeler ..... State University of Ohio
Dr. A. Ashley Weech ..... University of Cincinnati
Dr. William L. Bradford ..... University of Rochester
Dr. Tyree C. Wyatt ..... University of Syracuse
Dr. Sherman Little ..... University of Buffalo
Dr. Otto A. Faust ..... Albany Medical College
Dr. Frank Van Schoick ..... AAP, Michigan State Chairman
Dr. Edward A. Wishropp ..... Chairman, District V, AAP
Dr. John P. Hubbard ..... Director, Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Associate Director, Committee for the Improvement of Child Health

San Francisco, November 4, 1949

Dr. Francis Scott Smyth, Chairman ..... University of California
Dr. John A. Anderson ..... Stanford University
Dr. Arthur H. Parmelee ..... University of Southern California
Dr. Joseph B. Bilderback ..... University of Oregon
Dr. Walter B. Seelye ..... University of Washington
Dr. William C. Deamer ..... University of California
Dr. Milo B. Brooks ..... College of Medical Evangelists
Dr. Hertha Ehlers ..... College of Medical Evangelists
Dr. Donald Patterson ..... University of Vancouver
Dr. Crawford Bost ..... Chairman, District VIII, AAP
Dr. Frank H. Douglass ..... Alternate Chairman, District VIII, AAP
Dr. Morris L. Bridgeman ..... AAP, Oregon State Chairman
Dr. L. Paul Rasmussen ..... AAP, Utah State Chairman
Dr. Edward B. Shaw ..... President, American Academy of Pediatrics
Dr. Paul W. Beaven ..... President-elect, American Academy of Pediatrics
Dr. Robert S. Cleland ..... Los Angeles County Hospital
Dr. Hulda E. Thelander ..... Committee for the Improvement of Child Health
Dr. James L. Wilson ..... Committee for the Improvement of Child Health
Dr. John P. Hubbard ..... Director, Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Associate Director, Committee for the Improvement of Child Health

New York City, December 8, 1949

Dr. Samuel Z. Levine, Chairman ..... Cornell University
Dr. Allan M. Butler ..... Harvard University
Dr. Sidney Gellis ..... Harvard University
Dr. Rustin McIntosh ..... Columbia University
Dr. James M. Baty ..... Tufts College

Dr. Daniel C. Darrow ..... Yale University
Dr. Charles A. Weymuller ..... Long Island College
Dr. Ruel A. Benson ..... New York Medical College
Dr. Lawrence B. Slobody ..... New York Medical College
Dr. L. Emmett Holt, Jr. ..... New York University
Dr. Warren R. Sisson ..... President, AAP
Dr. Harry Bakwin ..... Chairman, District II, AAP
Dr. Thurman B. Givan ..... AAP, New York State Chairman
Dr. Frederick H. Wilke ..... AAP, New York State Chairman
Dr. George M. Wheatley ..... Committee for the Improvement of Child Health
Dr. John P. Hubbard ..... Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

Philadelphia, January 11, 1950

Dr. Waldo W. Nelson, Chairman ..... Temple University
Dr. Joseph Stokes, Jr. ..... University of Pennsylvania
Dr. Emily P. Bacon ..... Women's Medical College
Dr. Carl C. Fischer ..... Hahnemann Medical College
Dr. Edmund R. McCluskey ..... University of Pittsburgh
Dr. Francis F. Schwentker ..... Johns Hopkins University
Dr. J. Edmund Bradley ..... University of Maryland
Dr. Preston A. McLendon ..... George Washington University
Dr. Roland B. Scott ..... Howard University
Dr. Philip S. Barba ..... Chairman, District III, AAP
Dr. Theodore S. Wilder ..... AAP, Pennsylvania State Chairman
Dr. Hugh J. Davis ..... AAP, District of Columbia Chairman
Dr. Paul Harper ..... AAP, Maryland State Chairman
Dr. John McK. Mitchell ..... AAP, Committee on Education
Dr. John P. Hubbard ..... Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

Winston-Salem, January 27, 1950

Dr. Robert B. Lawson, Chairman ..... AAP, Committee on Education
Dr. Leroy J. Butler ..... Bowman Gray School of Medicine
Dr. Wilburt C. Davison ..... Duke University
Dr. Roger W. Dickson ..... Emory University
Dr. Philip A. Mulherin ..... University of Georgia
Dr. Mylnor W. Beach ..... Medical College of the State of South Carolina
Dr. Lee E. Sutton, Jr. ..... Medical College of Virginia
Dr. W. W. Waddell, Jr. ..... University of Virginia
Dr. Walter R. Berryhill ..... University of North Carolina
Dr. Charles R. Bugg ..... AAP, North Carolina State Chairman
Dr. Emily Gardner ..... AAP, Virginia State Chairman
Dr. John P. Hubbard ..... Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

Chicago, February 5, 1950

Dr. Henry G. Poncher, Chairman ..... University of Illinois
Dr. Francis H. Wright ..... University of Chicago
Dr. Maxwell P. Borovsky ..... Chicago Medical School
Dr. H. William Elghammer ..... Loyola University
Dr. John A. Bigler ..... Northwestern University
Dr. F. R. Janney ..... Marquette University
Dr. John M. Adams ..... University of Minnesota
Dr. John E. Gonce, Jr. ..... University of Wisconsin

Dr. Herman Jahr ..... University of Nebraska
Dr. Clifford G. Grulee ..... Secretary and Treasurer, AAP
Dr. Roger L. J. Kennedy ..... Chairman, District VI, AAP
Dr. John L. Reichert ..... AAP, Illinois State Chairman
Dr. John P. Hubbard ..... Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

Kansas City, Kan., March 9, 1950

Dr. Herbert C. Miller, Chairman ..... University of Kansas
Dr. J. Harry Murphy ..... Creighton University
Dr. Julian D. Boyd ..... State University of Iowa
Dr. John A. Lichty ..... University of Colorado
Dr. James F. Bosma ..... University of Utah
Dr. Alexis F. Hartmann ..... Washington University
Dr. Peter G. Danis ..... St. Louis University
Dr. William A. Reilly ..... University of Arkansas
Dr. James E. Dyson ..... AAP, Iowa State Chairman
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

New Orleans, April 7, 1950

Dr. Ralph V. Platou, Chairman ..... Tulane University
Dr. Clifford Grulee, Jr. ..... Tulane University
Dr. Myron E. Wegman ..... University of Louisiana
Dr. Sidney Chipman ..... University of Louisiana
Dr. Tom Mitchell ..... University of Tennessee
Dr. James Hughes ..... University of Tennessee
Dr. Amos Christie ..... Vanderbilt University
Dr. E. Perry Crump ..... Meharry Medical College
Dr. Harriett Bates ..... Southwestern Medical College
Dr. Arild E. Hansen ..... University of Texas
Dr. Theodore Panos ..... University of Texas
Dr. Clarence H. Webb ..... AAP, Louisiana State Chairman
Dr. Frank H. Lancaster ..... Committee for the Improvement of Child Health
Dr. Glidden L. Brooks ..... Committee for the Improvement of Child Health

APPENDIX B

Revised Evaluation Schedule

THIS revision is based on suggestions emerging from the series of meetings. The entire schedule is still in a formative stage, is therefore admittedly imperfect and is intended only as a more or less arbitrarily selected basis for the accumulation of data for further revisions.

EVALUATION SCHEDULE

DEPARTMENT OF PEDIATRICS SCHOOL .....

ADDRESS .....

DEPARTMENT HEAD ..... DEAN .....

ITEM	RATING BASIS	SCORE	
STAFF		OLD	REVISED
1. Independent department	yes	2	2
	no	0	0
2. Department head status	full time	8	5
	½ time or more	4	3
	¼ time or less	0	0
3. Full-time staff graduated 4 or more years ago	5 or more	10	3
	3-4	8	2
	1-2	4	1
	none	0	0
4. Ratio of students to full-time staff	25 or less		5
	25-35		4
	35-50		2
	50 or more		0
5. Ratio of pediatric teaching hours per week to students	2.00 or more	10	10
	1.50-2.00	8	8
	1.00-1.50	5	5
	.50-1.00	2	2
	less than .50	0	0
6. Students per instructor in O.P.D.	1-3	4	5
	3-5	2	3
	5-7	1	1
	more than 7	0	0
7. Per cent of staff certified or members of A.P.S., S.P.R., or A.A.P.	75-100	2	2
	50-75	1	1
	less than 50	0	0
8. Per cent of staff engaged in research	50-100	4	3
	25-50	2	2
	1-25	1	1
	none	0	0
FACILITIES FOR TEACHING			
9. Teaching service approved for pediatric residency training	yes	3	4
	no	0	0

ITEM	RATING BASIS	SCORE	
10. Beds under direct control of pediatric dept.:			
Newborn and premature bassinets	25 or more	2	3
	15-25	1	2
	less than 15	0	0
Children's beds	50 or more	2	6
	25-50	1	3
	less than 25	0	0
11. Beds under supervisory control of pediatric dept.:			
Newborn and premature bassinets	25 or more		2
	15-25		1
	less than 15		0
Children's beds	50 or more		2
	25-50		1
	less than 25		0
12. Total beds per student:			
Newborn and premature bassinets	1.00 or more	2	2
	.01-1.00	1	1
	less than .01	0	0
Children's beds	2.00 or more	4	4
	1.00-2.00	3	3
	.50-1.00	1	1
	less than .50	0	0
13. Total pediatric O.P.D. visits per student per year	100 or more	4	4
	50-100	2	2
	less than 50	0	0
CURRICULUM			
14. Actual hours in pediatrics during 4 years	400 or more	6	4
	300-400	4	3
	200-300	2	2
	less than 200	0	0
15. Clinical clerkship hours on general pediatric wards	150 or more		4
	100-150		3
	50-100		2
	less than 50		0
16. Clinical clerkship hours in O.P.D.	150 or more		4
	100-150		3
	50-100		2
	less than 50		0
17. In-patient histories taken by students	yes	2	2
	no	0	0
18. Out-patient histories taken by students	yes	2	2
	no	0	0
19. Students assigned to pediatrics without interruption	yes		1
	no		0
SPECIAL PEDIATRICS			
20. Is formal training given in care of newborn?	yes		1
	no		0
21. Is formal training given in care of well child?	yes		1
	no		0
22. Is formal training given in the acute communicable diseases of childhood?	yes		1
	no		0

ITEM	RATING BASIS		SCORE
23. Is formal training given in emotional problems?	yes		1
	no		0
24. Is formal training given in dental problems?	yes		1
	no		0
25. Is formal training given in problems of the handicapped, blind, deaf, speech defects, cerebral palsy, epilepsy?	all 6		2
	2 to 4		1
	none		0
26. Is instruction given in community problems, institutional problems, etc., e.g., foster care and adoption?	yes		1
	no		0
BUDGET			
27. Basic pediatric budget per student	$300 or more	5	9
	$200-$300	4	8
	$100-$200	2	4
	$ 50-$100	1	2
	less than $50	0	0
28. Supplementary budget (in thousands)	over 100		4
	50-100		3
	25-50		2
	10-25		1
	less than 10		0
SUMMARY			
Staff	Items 1-8	40	35
Clinical Facilities	Items 9-13	22	27
Curriculum	Items 14-26	27	25
Budget	Items 27-28	11	13

Old Score refers to the original rating used in the Study.

EXPLANATORY NOTES—EVALUATION SCHEDULE

DEFINITIONS

1. *Students* Unless otherwise indicated, the total number enrolled in the 3rd and 4th year classes in the medical school.
2. *Full-time* Major activities and responsibilities devoted to departmental functions (either teaching, research or administrative). Private practice, other than consultations, is excluded.
3. *Staff* Unless otherwise specified, the total number holding formal teaching or research positions in the department. Does not include hospital staff members unless they also have a departmental (school) appointment.
4. *Hours* Unless otherwise noted, only "catalogue hours"; time required of each student in pediatrics.
5. *Formal training* Implies *organized* instruction or experience in a subject rather than casual or chance exposure. This may be either required of all students or elective.
6. *Beds* Regularly assigned to children by the hospital *and* available for teaching purposes.

REFERENCES TO SPECIFIC ITEMS

Item 1: Full credit only if department is *directly* responsible to medical school administration. No credit if pediatrics is a subsidiary of internal medicine or other departments. In those instances where intraschool integration of teaching has necessarily lowered departmental barriers, full credit is assumed.

Item 2, 3: See definition of "full-time."

Item 4-6: See definition of "students."

Item 7, 8: See definition of "staff."

Item 5: In this item "hours" refers to total actual teaching hours by full and part-time staff; not merely catalogue hours. Also includes members of other departments, e.g., pathology, psychiatry, etc., teaching in the pediatric course.

Item 10: *Direct* control refers to responsibility and control of *medical care.*

Item 11: *Supervisory* control refers to non-medical as well as medical beds and implies consultative or other working arrangements which make beds available for pediatric teaching. Credit only where teaching is done by a member of the departmental staff. Do not include convalescent homes or domiciliary institutions.

APPENDIX C

Questions for Additional Discussion

THE following represent only a few of the problems about which both interest and concern were expressed at these meetings. It is evident that many more conferences and seminars will be necessary to develop satisfactory answers to the manifold questions faced by pediatric education.

1. Define the *basic* functions of a medical school department of pediatrics.
2. Relative significance and score value of each item of the evaluation schedule.
3. Over-all format and usefulness of the schedule.
4. The place of research in a pediatric department.
5. What are the implications to educational institutions of the changing character of pediatric practice?
6. What practical qualifications should be expected in a teacher of pediatrics? A department head?
7. Define more explicitly what is meant by a "full-time" teacher or department head.
8. How may "quality" of pediatric teaching be measured most accurately?
9. The problem of "integration" as it applies to pediatric teaching.
10. What facilities, clinical and otherwise, are necessary for effective teaching?
11. What staff is necessary for effective teaching?
12. What is a minimum (optimum) budget for a department of pediatrics?
13. How may funds for pediatric education be secured?
14. How much of the medical school curriculum (total hours) should be devoted to pediatrics?
15. When and how should pediatrics be introduced in the medical school curriculum?
16. What are the requirements for an effective clinical clerkship?
17. Importance, value, and methods of out-patient teaching.
18. Value and importance of the "block system" of assigning students for pediatric clinical clerkship.
19. Which and how much of the special fields of pediatrics should be taught at the undergraduate level?
20. How can care of the newborn be most safely and effectively taught?
21. How can the student be best oriented to his community responsibilities for child health?
22. The approach to the emotional problems of childhood.
23. A re-examination of present methods of teaching growth and development and "the well child."
24. Inquiry into pedagogical methods and aids to teaching.
25. Pediatric content of interne and resident training for general practice.
26. Content of pediatric residency training.
27. Post-graduate training in pediatrics.
28. Decentralization of graduate and postgraduate pediatric education.